STIC Search Report
Biotech-Chem Library

STIC Database Tracking Number: 166155

TO: Tamthom Truong
Location: rem/5B19/5C18
Art Unit: 1624
Sept 28, 2005

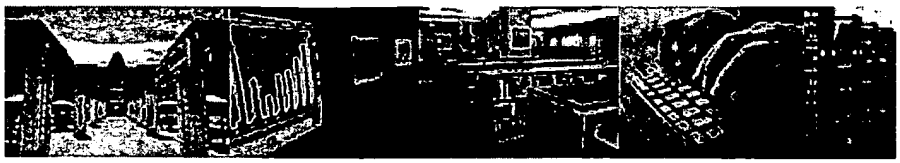
Case Serial Number: 10/016280

From: P. Sheppard
Location: Remsen Building
Phone: (571) 272-2529

sheppard@uspto.gov

Search Notes

Scientific & Technical Information Center



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( ) TC 2900 ( ) TC 3600 ( ) TC 3700 ( ) Law Lib ( ) Other

Your Contact Information:

* indicates mandatory information.

Your Name: TAMTHOM TRUONG
*Email Address: tamthom.truong@uspto.g
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*Employee No.: 74142
*Art Unit/Org.: 1624
*Office Location: REM 5B19
*Phone No.: x20676
Mailbox No.: REM 5C18

RECEIVED SEP 19 2005 TECH CENTER 1600/2900 (STIC)

*Case serial number: 10/ 016,280
If not related to a patent application, please enter NA here.

Class / Subclass(es): 544/293 546/159 514/266.4, 313

Earliest Priority Filing Date: 06-21-1999

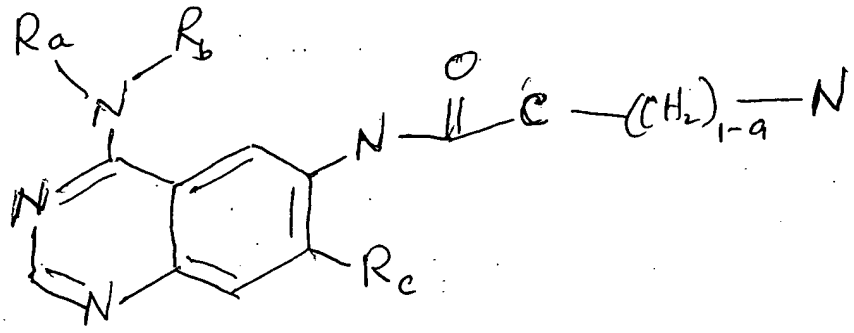
Format preferred for results:

☑ Paper ☐ Diskette ☐ E-mail

Provide detailed information on your search topic: See attached query

- In your own words, describe in detail the concepts or subjects you want us to se
- Include synonyms, keywords, and acronyms. Define terms that have special me
- *For Chemical Structure Searches Only*
  Include the elected species or structures, keywords, synonyms, acronyms, and
- *For Sequence Searches Only*
  Include all pertinent information (parent, child, divisional, or issued patent numb serial number.
- *For Foreign Patent Family Searches Only*
  Include the country name and patent number.

10/016,280 Query



R_a = H, Ak

R_b = phenyl, benzyl or 1-phenylethyl (opened for substitution)

R_c = -O-Ak or -O-Cy (opened for substitution)

C = $-CH=C=CH-$, $>C=CH_2-$, $-CH=CH-$, $-C\equiv C-$, $-CH=CH-CH=CH-$

See also attached claim 18

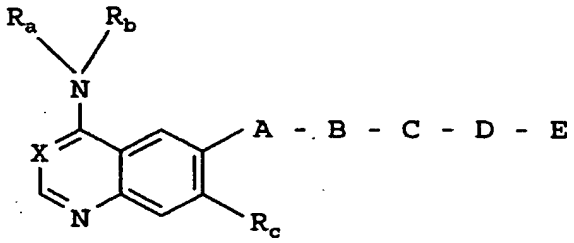
Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

Claims 1-13 (canceled)

Claim 14 (new) A quinazoline compound of formula



, (I)

wherein

R_a denotes a hydrogen atom or a C_{1-4}-alkyl group,

R_b denotes a phenyl, benzyl or 1-phenylethyl group wherein the phenyl nucleus is substituted in each case by the groups R_1 to R_3, whilst

R_1 and R_2, which may be identical or different, in each case denote a hydrogen, fluorine, chlorine, bromine or iodine atom,

a C_{1-4}-alkyl, hydroxy, C_{1-4}-alkoxy, C_{3-6}-cycloalkyl, C_{4-6}-cycloalkoxy, C_{2-5}-alkenyl or C_{2-5}-alkynyl group,

an aryl, aryloxy, arylmethyl or arylmethoxy group,

a C_{3-5}-alkenyloxy or C_{3-5}-alkynyloxy group, whilst the unsaturated moiety may not be linked to the oxygen atom,

a C_{1-4}-alkylsulfenyl, C_{1-4}-alkylsulfinyl, C_{1-4}-alkylsulfonyl, C_{1-4}-alkylsulfonyloxy, trifluoromethylsulfenyl, trifluoromethylsulfinyl or trifluoromethylsulfonyl group,

a methyl or methoxy group substituted by 1 to 3 fluorine atoms,

an ethyl or ethoxy group substituted by 1 to 5 fluorine atoms,

a cyano or nitro group or an amino group optionally substituted by one or two C_{1-4}-alkyl groups, wherein the substituents may be identical or different, or

R_1 together with R_2, if they are bound to adjacent carbon atoms, denote a -CH=CH-CH=CH group and

R_3 denotes a hydrogen, fluorine, chlorine or bromine atom,

a C_{1-4}-alkyl, trifluoromethyl or C_{1-4}-alkoxy group,

X denotes a nitrogen atom,

A denotes an imino group optionally substituted by a C_{1-4}-alkyl group,

B denotes a carbonyl group,

C denotes a -CH=C=CH-, $>C=CH_2$ or -CH=CH- group which may be substituted in each case by one or two methyl groups or by a trifluoromethyl group,

an -C≡C- group or

a -CH=CH-CH=CH- group optionally substituted by 1 to 4 methyl groups or by a trifluoromethyl group,

D denotes an alkylene group wherein the alkylene moiety contains 1 to 8 carbon atoms and additionally 1 to 4 hydrogen atoms in the alkylene moiety may be replaced by fluorine atoms,

E denotes an amino, C_{1-4}-alkylamino or di-(C_{1-4}-alkyl)-amino group wherein the alkyl moieties may be identical or different,

a C_{2-4}-alkylamino group wherein the alkyl moiety is substituted in β-, γ-, or δ-position with regard to the nitrogen atom of the amino group by the group R_5, whilst

R_5 denotes a hydroxy, C_{1-4}-alkoxy, amino, C_{1-4}-alkylamino or di-(C_{1-4}-alkyl)-amino group,

an N-(C_{1-4}-alkyl)-N-(C_{2-4}-alkyl)-amino group wherein the C_{2-4}-alkyl moiety is substituted in β-, γ-, or δ-position with regard to the nitrogen atom of the amino group by the group R_5, whilst R_5 is as hereinbefore defined,

a di-(C_{2-4}-alkyl)-amino group wherein the two C_{2-4}-alkyl moieties are substituted in each case in β-, γ-, or δ-position with regard to the nitrogen atom of the amino group by the group R_5, whilst the substituents may be identical or different and R_5 is as hereinbefore defined,

a C_{3-7}-cycloalkylamino or C_{3-7}-cycloalkyl-C_{1-3}-alkylamino group wherein in each case the nitrogen atom may be substituted by a further C_{1-4}-alkyl group,

R_c denotes a C_{4-7}-cycloalkoxy or C_{3-7}-cycloalkyl-C_{1-6}-alkoxy group wherein the cycloalkyl moiety in each case may be substituted by a C_{1-3}-alkyl, hydroxy, C_{1-4}-alkoxy, amino, C_{1-4}-alkylamino, di-(C_{1-4}-alkyl)-amino, hydroxy-C_{1-2}-alkyl, C_{1-4}-alkoxy-C_{1-2}-alkyl, amino-C_{1-2}-alkyl, C_{1-4}-alkylamino-C_{1-2}-alkyl, or di-(C_{1-4}-alkyl)-amino-C_{1-2}-alkyl group, whilst the abovementioned monosubstituted cycloalkyl moieties may additionally be substituted by a C_{1-3}-alkyl group,

whilst

by the aryl moieties mentioned in the definition of the abovementioned groups is meant a phenyl group which in each case may be monosubstituted by R_7, mono-, di- or trisubstituted by R_8 or monosubstituted by R_7 and additionally mono- or disubstituted by R_8, wherein the substituents may be identical or different and

R_7 denotes a cyano, carboxy, C_{1-4}-alkoxycarbonyl, aminocarbonyl, C_{1-4}-alkylaminocarbonyl, di-(C_{1-4}-alkyl)-aminocarbonyl, C_{1-4}-alkylsulfenyl, C_{1-4}-alkylsulfinyl, C_{1-4}-alkylsulfonyl, hydroxy, C_{1-4}-alkylsulfonyloxy, trifluoromethyloxy, nitro, amino, C_{1-4}-alkylamino, di-(C_{1-4}-alkyl)-amino, C_{1-4}-alkyl-carbonylamino, N-(C_{1-4}-alkyl)-C_{1-4}-alkylcarbonylamino, C_{1-4}-alkylsulfonylamino, N-(C_{1-4}-alkyl)-C_{1-4}-alkylsulfonylamino, aminosulfonyl, C_{1-4}-alkylaminosulfonyl or di-(C_{1-4}-alkyl)-aminosulfonyl group, and

R_8 denotes a fluorine, chlorine, bromine or iodine atom, a C_{1-4}-alkyl, trifluoromethyl or C_{1-4}-alkoxy group or

two groups R_8, if they are bound to adjacent carbon atoms, together denote a C_{3-5}-alkylene or 1,3-butadien-1,4-ylene group,

or the tautomers, or stereoisomers or pharmaceutically acceptable salts thereof.

~~Claim 15 (new) The quinazoline of formula I according to claim 14~~, wherein

R_a denotes a hydrogen atom,

R_b denotes a phenyl, benzyl or 1-phenylethyl group wherein the phenyl nucleus is substituted in each case by the groups R_1 to R_3, whilst

R_1 and R_2, which may be identical or different, in each case denote a hydrogen, fluorine, chlorine, bromine or iodine atom,

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=> d his ful

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L4            36 SEA SSS SAM L3
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L7           214 SEA SUB=L5 SSS FUL L6

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L10           24 SEA ABB=ON  PLU=ON  L9
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L14           61 SEA ABB=ON  PLU=ON  ("METZ T"/AU OR "METZ T D"/AU OR "METZ T
                 E"/AU OR "METZ T O"/AU) OR ("METZ THOMAS"/AU OR "METZ THOMAS
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L15          163 SEA ABB=ON  PLU=ON  ("JUNG B"/AU OR "JUNG B C"/AU OR "JUNG B
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                 S"/AU OR "JUNG B T"/AU OR "JUNG B Y"/AU) OR "JUNG BIRGIT"/AU
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FILE HOME

FILE REGISTRY
Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 27 SEP 2005 HIGHEST RN 864057-55-6
DICTIONARY FILE UPDATES: 27 SEP 2005 HIGHEST RN 864057-55-6

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*                                                                    *
* The CA roles and document type information have been removed from  *
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* effective March 20, 2005.  A new display format, IDERL, is now     *
* available and contains the CA role and document type information.  *
*                                                                    *
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Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
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FILE HCAPLUS

FILE COVERS 1907 - 28 Sep 2005 VOL 143 ISS 14
FILE LAST UPDATED: 27 Sep 2005 (20050927/ED)

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=> fil hcaplus
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This file contains CAS Registry Numbers for easy and accurate
substance identification.

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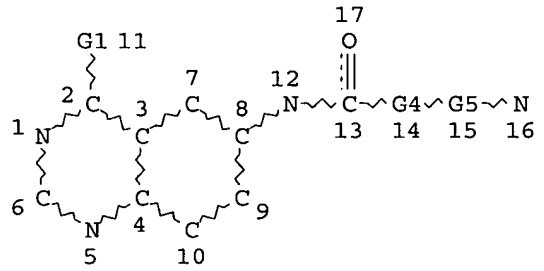
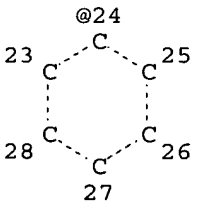
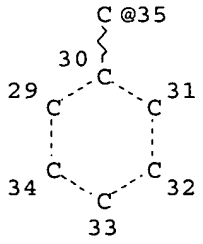
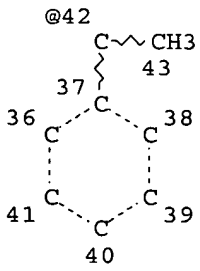
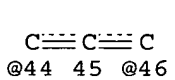
L3 STR

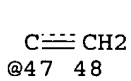


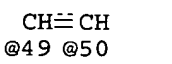


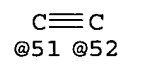


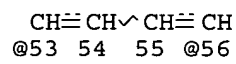












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NUMBER OF NODES IS 56

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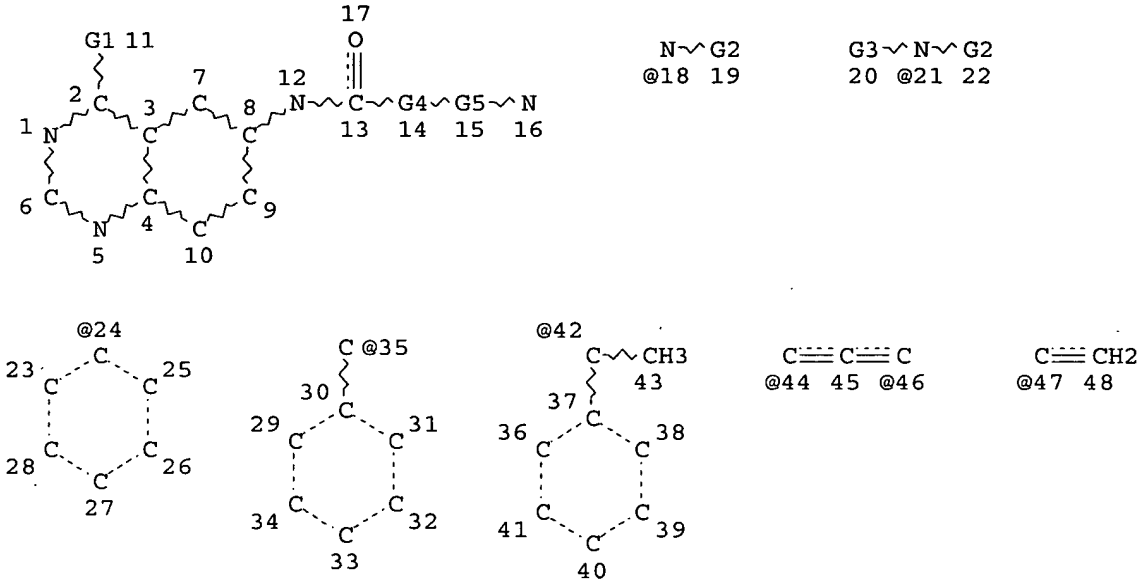

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=> d ibib abs hitstr l22 1-34

L22  ANSWER 1 OF 34  HCAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         2005:1005982  HCAPLUS
TITLE:                    Imidazopyridazinediones, their preparation and their
                          use as pharmaceutical compositions
INVENTOR(S):              Eckhardt, Matthias; Himmelsbach, Frank;
                          Kauffmann-Hefner, Iris; Langkopf, Elke;
                          Tadayyon, Mohammad; Thomas, Leo
PATENT ASSIGNEE(S):       Boehringer Ingelheim International G.m.b.H., Germany
SOURCE:                   U.S. Pat. Appl. Publ., 29 pp.
                          CODEN: USXXCO
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     --------------       ----   --------    --------------------    --------
     US 2005203095         A1    20050915    US 2005-75791           20050309
     WO 2005087774         A1    20050922    WO 2005-EP2524          20050309
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             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
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             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM,
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AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: DE 2004-102004012366A 20040313
US 2004-561321P P 20040412

AB The invention relates to substituted imidazopyridazinediones of general formula wherein R1 and R4 are defined as in claim 1, the tautomers, the enantiomers, the diastereomers, the mixts. thereof and the salts thereof, which have valuable pharmacol. properties, particularly an inhibiting effect on the activity of the enzyme dipeptidyl-peptidase-IV (DPP-IV).

L22 ANSWER 2 OF 34 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:1004745 HCAPLUS
TITLE: 8-[3-amino-piperidin-1-yl]-xanthine, the production thereof and the use in the form of a dpp inhibitor
INVENTOR(S): **Himmelsbach, Frank; Langkopf, Elke** ; Eckhardt, Matthias; Tadayyon, Mohammad; Thomas, Leo
PATENT ASSIGNEE(S): Boehringer Ingelheim International G.m.b.H., Germany; Boheringer Ingelheim Pharma G.m.b.H. & Co. K.-G.
SOURCE: PCT Int. Appl., 82 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005085246	A1	20050915	WO 2005-EP1427	20050212
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
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DE 102004008112	A1	20050901	DE 2004-102004008112	20040218

PRIORITY APPLN. INFO.: DE 2004-102004008112A 20040218
DE 2004-102004012921A 20040317
DE 2004-102004032263A 20040703

AB The invention relates to substituted xanthines of general formula (I), wherein R is such as defined in claim 1, and to the tautomers, stereoisomers, mixtures and the salts thereof, said products exhibiting precious pharmacological properties, in particular an inhibiting effect on a dipeptidylpeptidasa-IV (DPP-IV) enzyme activity.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 3 OF 34 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:959677 HCAPLUS
TITLE: Method for the production of 8-[3-aminopiperidin-1-yl]xanthines and their use as drugs
INVENTOR(S): **Himmelsbach, Frank; Langkopf, Elke** ; Eckhardt, Matthias; Tadayyon, Mohammad; Thomas, Leo
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma GmbH & Co. Kg, Germany

SOURCE: Ger. Offen., 24 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 102004008112	A1	20050901	DE 2004-102004008112	20040218
WO 2005085246	A1	20050915	WO 2005-EP1427	20050212

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PRIORITY APPLN. INFO.:
DE 2004-102004008112A 20040218
DE 2004-102004012921A 20040317
DE 2004-102004032263A 20040703

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention concerns substituted xanthines I [R = CH2Ph, CH2C6H4F-2, CH2C6H4F-3, CH2C6H4F-4, CH2C6H4Cl-2, CH2C6H4Cl-3, CH2C6H4Cl-4, CH2C6H4CF3-2, CH2C6H4CF3-3, CH2C6H4CF3-4, CH2C6H4CN-2, CH2C6H4CN-3, CH2C6H4CN-4, CH2C6H3(CN)2-2,6, CH2C6H3(CN)2-3,4, CH2C6H3(CN)2-3,5, CH2C6H3CN-4-CF3-2, CH2C6H3CN-4-NO2-3, CH2C6H3CN-2-OMe-4, CH2C6H3CN-2-OMe-5, CH2C6H3CN-2-F-4, CH2C6H3CN-2-F-5, CH2C6H3CN-2-F-6, CH2C6H3CN-3F-4, CH2C6H3CN-4-F-2, CH2C6H3CN-2-Cl-3, CH2C6H3CN-4-Cl-2, CH2C6H3CN-2-Br-4, CH2C6H4OMe-2, CH2C6H4OMe-3, CH2C6H4OMe-4, CH2C6H3(OMe)2-3,4, CH2C6H3(OMe)2-3,5, 3,4-dimethoxy-6-fluorobenzyl, (benzo[1,3]dioxol-5-yl)methyl, 2-(3-(cyclopropyloxy)phenyl)-2-oxoethyl, 2-(3-(cyclopropylmethoxy)phenyl)-2-oxoethyl,2-(3-(cyclobutyloxy)phenyl)-2-oxoethyl, 2-oxo-2-[2-(pyridin-3-yl)phenyl]ethyl, 2-oxo-2-[2-(pyridin-4-yl)phenyl]ethyl, (3-cyanonaphth-1-yl)methyl, (1,4-dicyanonaphth-1-yl)methyl, (2,4-dimethoxynaphth-1-yl)methyl, (pyridin-2-yl)methyl, (6-fluoropyridin-2-yl)methyl, (5-methoxypyridin-2-yl)methyl, (3-cyanopyridin-2-yl)methyl, (6-cyanopyridin-2-yl)methyl, (5-cyanopyridin-2-yl)methyl, (4-cyanopyridin-2-yl)methyl, (4-cyanopyridin-3-yl)methyl, (3-cyanopyridin-4-yl)methyl, (2-cyanopyridin-3-yl)methyl, (2-cyanopyridin-4-yl)methyl, etc.], their tautomers, enantiomers, stereoisomers, mixts. and physiol. acceptable salts, which contain valuable pharmacol. characteristics, in particular an inhibiting effect on the activity of the enzyme dipeptidylpeptidase IV (DPP-IV). The procedure for the preparation of I comprises: (a) reaction of xanthine II [Z1 = leaving group, e.g., substituted OH, SH, sulfinyl, sulfonyl, sulfonyloxy] with 3-(Boc-amino)piperidine (Boc = CO2CMe3); and (b) deprotection of [3-(Boc-amino)piperidin-1-yl]xanthine III. Thus, 1-[(4-(phenylamino)quinazolin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-[3-aminopiperidin-1-yl]xanthine (IV) was prepared from 3-methyl-7-(2-butyn-1-

yl)-8-[3-(Boc-amino)piperidin-1-yl]xanthine via regioselective N-alkylation with 2-(chloromethyl)-4-(phenylamino)quinazoline in DMF containing Cs2CO3 followed by deprotection in CH2Cl2 containing HCl in Me2CHOH. The enzyme-inhibiting effect of IV was determined [IC50 = 6 nM]. Drug dosage forms containing I are prepared (dragees, tablets, suppositories, hard-gelatin capsules, suspensions and ampules).

L22 ANSWER 4 OF 34 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:904341 HCAPLUS
DOCUMENT NUMBER: 143:229652
TITLE: Preparation of 8-[3-amino-piperidin-1-yl]-xanthines for use in pharmaceutical compositions that inhibit the activity of dipeptidylpeptidase-IV (DPP-IV)
INVENTOR(S): **Himmelsbach, Frank; Langkopf, Elke**; Eckhardt, Matthias; Tadayyon, Mohammad; Thomas, Leo
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma GmbH & Co. KG, Germany
SOURCE: U.S. Pat. Appl. Publ., 14 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005187227	A1	20050825	US 2005-62518	20050222
DE 102004009039	A1	20050908	DE 2004-102004009039	20040223
WO 2005082906	A1	20050909	WO 2005-EP1587	20050217

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: DE 2004-102004009039A 20040223
US 2004-551752P P 20040310

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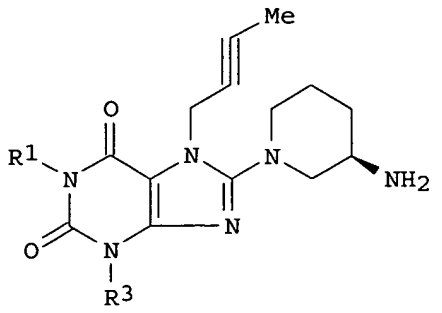

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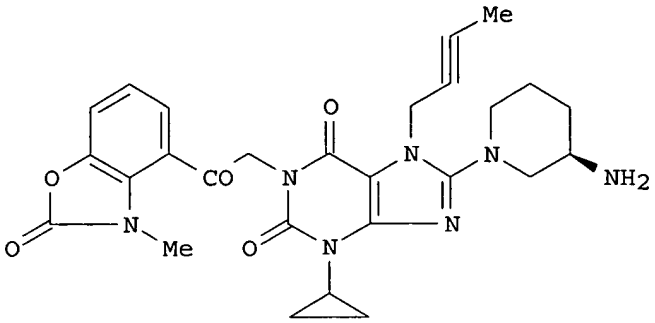

II

AB Xanthine derivs., such as I [R1 = benzyl, pyridinylmethyl, quinoxalinylmethyl, quinolinylmethyl, etc.; R3 = Ph, cyclohexyl], were prepared for therapeutic use as DPP-IV inhibitors and were claimed for use in the treatment of type I diabetes mellitus, type II diabetes mellitus, arthritis, obesity, allograft transplantation and osteoporosis caused by calcitonin. Thus, xanthine derivative II was prepared via an N-alkylation reaction of 3-cyclopropyl-7-(2-butyn-1-yl)-8-[(R)-3-(tert-butyloxycarbonylamino)piperidin-1-yl]xanthine with 4-(2-bromoacetyl)-3-methyl-3H-benzoxazol-2-one and subsequent amino deprotection. Pharmaceutical formulations containing the prepared xanthine derivs. were presented.

L22 ANSWER 5 OF 34 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:570898 HCAPLUS
DOCUMENT NUMBER: 143:78214
TITLE: Preparation of (homo)piperazinylimidazoyridazinones for treatment of diabetes mellitus.
INVENTOR(S): **Himmelsbach, Frank**; Hauel, Norbert; **Langkopf, Elke**; Eckhardt, Matthias; Kauffmann-Hefner, Iris; Tadayyon, Mohammad; Thomas, Leo
PATENT ASSIGNEE(S): Boehringer Ingelheim International G.m.b.H., Germany; Boehringer Ingelheim Pharma G.m.b.H. & Co. KG
SOURCE: PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005058901	A1	20050630	WO 2004-EP14125	20041211

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

DE 10359098	A1	20050728	DE 2003-10359098	20031217
US 2005171093	A1	20050804	US 2004-16176	20041217
PRIORITY APPLN. INFO.:			DE 2003-10359098	A 20031217
			US 2004-538555P	P 20040123

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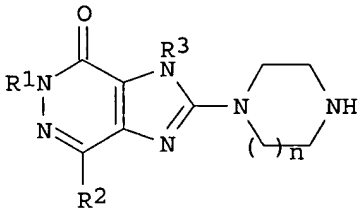

I

AB Title compds. [I; R1 = (substituted) heteroarylalkyl, naphthylalkyl; R2 = H, Me; R3 = 2-butyn-1-yl, 1-buten-1-yl, 2-buten-1-yl, 3-methyl-2-buten-1-yl], were prepared Thus, 2-bromo-3-(2-butyn-1-yl)-5-[(4-methylquinazolin-2-yl)methyl]-3,5-dihydroimidazo[4,5-d]pyridazin-4-one (preparation given) and piperazine were microwaved in DMF at 200° for 5 min. to give 51% 2-(piperazin-1-yl)-3-(2-butyn-1-yl)-5-[(4-methylquinazolin-2-yl)methyl]-3,5-dihydroimidazo[4,5-d]pyridazin-4-one. The latter inhibited dipeptidylpeptidase-IV with IC50 = 5 nM.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 6 OF 34 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:	2005:570533 HCAPLUS
DOCUMENT NUMBER:	143:97364
TITLE:	Bicyclic imidazole derivatives, the preparation thereof and their use as pharmaceutical compositions
INVENTOR(S):	**Himmelsbach, Frank; Langkopf, Elke**; Eckhardt, Matthias; Hauel, Norbert; Tadayyon, Mohammad; Thomas, Leo
PATENT ASSIGNEE(S):	Boehringer Ingelheim International G.m.b.H., Germany
SOURCE:	U.S. Pat. Appl. Publ., 17 pp. CODEN: USXXCO
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005143377	A1	20050630	US 2004-18894	20041221
DE 10360835	A1	20050721	DE 2003-10360835	20031223

WO 2005063750 A1 20050714 WO 2004-EP14399 20041217
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
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PRIORITY APPLN. INFO.: DE 2003-10360835 A 20031223
US 2004-538684P P 20040123
DE 2004-102004046530A 20040924

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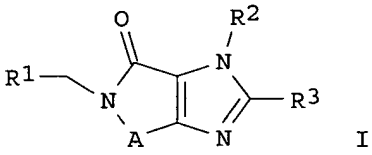

I

AB The present invention relates to bicyclic imidazole compds. of general formula I wherein R1 to R3 and A are defined in claims (an example of a compound of the invention is 1-[(4-methyl-3-oxyquinazolin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-((R)-3-aminopiperidin-1-yl)xanthine), , the tautomers, the enantiomers, the stereoisomers, the mixts. thereof and the salts thereof, which have valuable pharmacol. properties, particularly an inhibiting effect on the activity of the enzyme dipeptidylpeptidase-IV (DPP-IV). In addition to the compds., pharmaceutical compns. containing I and a process for preparing I are also claimed. A method of treating a disease chosen from type I and II diabetes mellitus, arthritis, obesity, allograft transplantation and calcitonin-induced osteoporosis using I is also claimed.

L22 ANSWER 7 OF 34 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:490367 HCAPLUS
DOCUMENT NUMBER: 143:26630
TITLE: Preparation of 8-(piperazine-1-yl)xanthines and related compounds as dipeptidylpeptidase-IV (DPP-IV) inhibitors
INVENTOR(S): **Himmelsbach, Frank; Langkopf, Elke**; Eckhardt, Matthias; Tadayyon, Mohammad; Thomas, Leo
PATENT ASSIGNEE(S): Boehringer Ingelheim International G.m.b.H., Germany; Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G.
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

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     WO 2005051950         A1     20050609     WO 2004-EP13144         20041119
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     DE 10355304           A1     20050623     DE 2003-10355304        20031127
     US 2005130985         A1     20050616     US 2004-979468          20041102
PRIORITY APPLN. INFO.:                          DE 2003-10355304     A  20031127
                                                US 2003-530560P      P  20031218

OTHER SOURCE(S):          MARPAT 143:26630
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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [X = (CH2)n; n = 1, 2; R1 = heteroaryl, e.g., phenylpyrimidinyl, quinolinyl, isoquinolinyl, etc.; R2 = CH3, Et, Pr, etc.; R3 = 2-butyn-1-yl, 1-buten-1-yl, 2-buten-1-yl, etc.] and their pharmaceutically acceptable salts and formulations were prepared For example, condensation of piperazine and bromoxanthine II, afforded claimed piperazinylxanthine III in 66% yield. In dipeptidylpeptidase-IV (DPP-IV) inhibition assays, 4-examples of compds. I exhibited IC50 values ranging from 3-17 nM, e.g., the IC50 value of piperazinylxanthine III was 3 nM. Compds. I are claimed to be useful for the treatment of type I and type II diabetes.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 8 OF 34 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:284142 HCAPLUS
DOCUMENT NUMBER: 142:355278
TITLE: Preparation of quinazolines and other bicyclic heterocycles and their use as medicaments
INVENTOR(S): **Himmelsbach, Frank; Jung, Birgit**
PATENT ASSIGNEE(S): Boehringer Ingelheim International GmbH, Germany
SOURCE: U.S. Pat. Appl. Publ., 23 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

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     PATENT NO.            KIND   DATE         APPLICATION NO.          DATE
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     US 2005070560          A1    20050331     US 2004-947854           20040923
     DE 10345875            A1    20050421     DE 2003-10345875         20030930
     WO 2005033096          A1    20050414     WO 2004-EP10723          20040924
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SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
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PRIORITY APPLN. INFO.: DE 2003-10345875 A 20030930
US 2003-514799P P 20031027

OTHER SOURCE(S): MARPAT 142:355278

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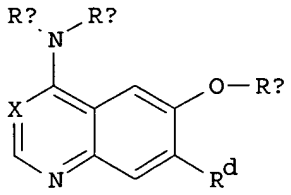

I

AB The invention relates to compds. I [Ra is H or alkyl; Rb is 1-phenylethyl in which the Ph ring may be substituted; Rc is C4-C6 cycloalkyl which may be substituted by amino groups, optionally 1-substituted azetidin-3-yl, pyrrolidin-3-yl or piperidin-3(or 4)-yl, tetrahydrofuran-3-yl, tetrahydropyran-3(or 4)-yl; Rd is OH, alkoxy, fluoromethoxy, fluoroethoxy, tetrahydrofuran-3-yl, tetrahydropyran-3(or 4)-yl, etc.; X is N, or NC-C] which have an inhibitory action on signal transduction mediated by tyrosine kinases and are useful for the treatment of oncosis and benign prostate hyperplasia (BPH) and diseases of the lung and the airways. Thus, (R)-4-(1-phenylethylamino)-6-(piperidin-4-yloxy)-7-methoxyquinazoline dihydrochloride was prepared by etherification of (R)-4-(1-phenylethylamino)-6-hydroxy-7-methoxyquinazoline with 1-(tert-butoxycarbonyl)-4-(p-toluenesulfonyloxy)piperidine, followed by by deprotection with 5 M isopropanolic hydrochloric acid in methylene chloride.

L22 ANSWER 9 OF 34 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:1127381 HCAPLUS
DOCUMENT NUMBER: 142:74585
TITLE: Preparation of imidazopyridazinones and related compounds as dipeptidyl peptidase IV (DPP-IV) inhibitors for the treatment of diabetes
INVENTOR(S): Eckhardt, Matthias; Hauel, Norbert; **Langkopf, Elke**; **Himmelsbach, Frank**; Kauffmann-Hefner, Iris; Tadayyon, Mohammad; Mark, Michael
PATENT ASSIGNEE(S): Boehringer Ingelheim International GmbH, Germany; Boehringer Ingelheim Pharma GmbH & Co. Kg
SOURCE: PCT Int. Appl., 106 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2004111051	A1	20041223	WO 2004-EP6303	20040611
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10327439	A1	20050105	DE 2003-10327439	20030618
US 2005026921	A1	20050203	US 2004-865719	20040610
PRIORITY APPLN. INFO.:			DE 2003-10327439 A	20030618
			US 2003-487309P P	20030715

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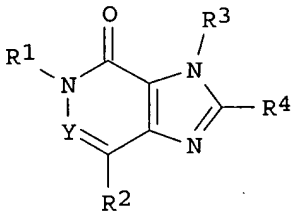

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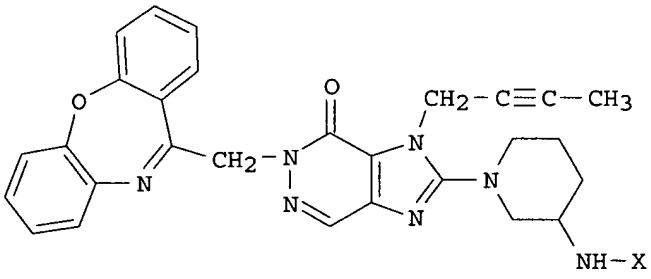

II

AB Title compds. I [R1 = alkyl substituted 3,4-dihydroquinolinyl, 3,4-dihydroisoquinolinyl, 1,4-dihydroquinazolinyl, etc.; R2 = H, F, Cl, etc.; R3 = (un)substituted alkyl, e.g., cycloalkyl, cycloalkenyl, aryl, etc.; R4 = (un)substituted azetidin-1-yl, pyrrolidin-1-yl; Y = N, C-R5; R5 = H, alkyl] and their pharmaceutically acceptable salts and formulations were prepared For example, TFA mediated deprotection of Boc-amine II (X = Boc) afforded claimed imidazopyridazinone II (X = H) in 63% yield. In dipeptidyl peptidase IV (DPP-IV) inhibition assays, 8-examples of compds. I exhibited IC50 values ranging from 3-58 nM, e.g., the IC50 value of imidazopyridazinone II (X = H) was 14 nM. Compds. I are claimed to be useful for the treatment of type I and type II diabetes mellitus.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 10 OF 34 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:1074187 HCAPLUS

DOCUMENT NUMBER: 142:56336
TITLE: Preparation of 4-anilinoquinazolines as inhibitors of tyrosine kinase-mediated signal transduction
INVENTOR(S): **Himmelsbach, Frank**; Soyka, Rainer; **Jung, Birgit**
PATENT ASSIGNEE(S): Boehringer Ingelheim International G.m.b.H., Germany; Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G.
SOURCE: PCT Int. Appl., 53 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004108664	A2	20041216	WO 2004-EP5965		20040602
WO 2004108664	A3	20050526			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
DE 10326186	A1	20041223	DE 2003-10326186		20030606
US 2005014772	A1	20050120	US 2004-860453		20040603
PRIORITY APPLN. INFO.:			DE 2003-10326186	A	20030606
			US 2003-480720P	P	20030623

OTHER SOURCE(S): MARPAT 142:56336
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [R1 = H, alkyl; R2 = (un)substituted Ph, 1-phenylethyl; R3 = (un)substituted (2-hydroxyethyl)amino with provisos; R4 = H, OH, alkoxy, etc.; X =] and their pharmaceutically acceptable salts and formulations were prepared For example, thionyl chloride mediated coupling of quinazoline II. i.e., prepared from 3,4-dihydro-4-oxo-6-acetyloxy-7-methoxyquinazoline in 4-steps, and 3-chloro-4-fluoroaniline afforded claimed anilinoquinazoline III in 64% yield. Compds. I are claimed to be useful for the treatment of tumor diseases, especially benign prostatic hyperplasia.

L22 ANSWER 11 OF 34 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:906864 HCAPLUS
DOCUMENT NUMBER: 142:392
TITLE: Inhibition of epidermal growth factor receptor activity by two pyrimidopyrimidine derivatives
AUTHOR(S): Solca, Flavio F.; **Baum, Anke**; **Langkopf, Elke**; Dahmann, Georg; Heider, Karl-Heinz; **Himmelsbach, Frank**; van Meel, Jacques C. A.
CORPORATE SOURCE: Department of New Chemical Entities Pharmacology,

Boehringer Ingelheim, Vienna, Austria
SOURCE: Journal of Pharmacology and Experimental Therapeutics (2004), 311(2), 502-509
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Overexpression of the epidermal growth factor receptors (EGFRs) and human epidermal growth factor receptor 2 occurs frequently in human cancers and is associated with aggressive tumor behavior and poor patient prognosis. We have investigated the effects in vitro and in vivo of a new class of inhibitor mols. on the growth of several human cancer cell lines, BIBX1382 [N8-(3-chloro-4-fluoro-phenyl)-N2-(1-methyl-piperidin-4-yl)-pyrimido[5,4-d]pyrimidine-2,8-diamine] and BIBU1361 [(3-chloro-4-fluoro-phenyl)-[6-(4-diethylaminomethyl-piperidin-1-yl)-pyrimido[5,4-d]pyrimidin-4-yl]-amine] are two new selective EGFR kinase inhibitors that do not block the activity of other tyrosine kinases. BIBU1361 blocked epidermal growth factor-induced phosphorylation of EGFR and also prevented downstream responses such as mitogen-activated protein kinase kinase (MAPK/extracellular signal-regulated kinase kinase) and MAPK activation in cells. In accordance with these observations thymidine incorporation into EGFR-expressing KB cells was selectively and potently inhibited by BIBX1382 and BIBU1361 with half-maximally EDs in the nanomolar range. Oral administration of these compds. inhibited the growth of established human xenografts in athymic mice, including vulval and head and neck squamous cell carcinomas. Tumor growth inhibition by BIBX1382 coincided with reduced pEGFR and Ki-67 levels in vivo, which is in accordance with the expected effect of EGFR inhibitors. Collectively, these results show that the structural class of pyrimidopyrimidines, exemplified here by BIBX1382 and BIBU1361, represents an interesting scaffold for the design of EGFR inhibitors.

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 12 OF 34 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:493705 HCAPLUS
DOCUMENT NUMBER: 141:54352
TITLE: Production and use of novel substituted imidazopyridinones and imidazopyridazones as medicaments
INVENTOR(S): Hauel, Norbert; **Himmelsbach, Frank**; **Langkopf, Elke**; Eckhardt, Matthias; Maier, Roland; Mark, Michael; Tadayyon, Mohammad; Kauffmann-Hefner, Iris
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G., Germany
SOURCE: PCT Int. Appl., 123 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004050658	A1	20040617	WO 2003-EP13648	20031203
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,				

LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO,
NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ,
TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK,
TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

DE 10256264	A1	20040624	DE 2002-10256264 20021203
DE 10309927	A1	20040916	DE 2003-10309927 20030307
US 2005020574	A1	20050127	US 2003-726214 20031202
CA 2508233	AA	20040617	CA 2003-2508233 20031203
EP 1569936	A1	20050907	EP 2003-789123 20031203

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

PRIORITY APPLN. INFO.:

DE 2002-10256264	A	20021203
DE 2003-10309927	A	20030307
US 2002-437438P	P	20021230
US 2003-456598P	P	20030321
WO 2003-EP13648	W	20031203

OTHER SOURCE(S): MARPAT 141:54352

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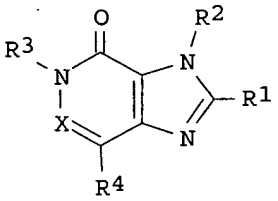

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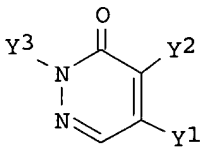
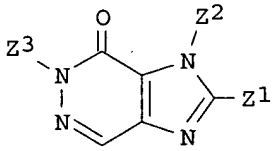


II



III

AB The invention relates to substituted imidazo-pyridinones and imidazo-pyridazinones I [R1 = 5- to 7-membered cycloalkylenimino (optionally substituted with C1-3-alkyl), 6- to 7-membered cycloalkylenimino (4-methylene substituted, to 7-membered cycloalkylamino, etc.; R2 = CH2Ph (F-, Cl-, Br-, CN-substituted Ph), (un)branched C3-8-alkenyl, C3-5-alkynyl, C3-7-cycloalkylmethyl, C5-7-cycloalkylmethyl, urylmethyl, thienylmethyl, pyrrolylmethyl, thiazolylmethyl, ; R3 = (un)branched C1-6-alkyl, C1-6-haloalkyl, C1-6-cyanoalkyl, CHMePh, CH2CH(OH)Ph, CH2COPh (optionally substituted Ph), 3-methyl-2-oxo-2,3-dihydrobenzoxazolyl)carbonylmethyl, thienylcarbonylmethyl, mono- or bicyclic heteroaryl-(C1-6-alkyl); R4 = H, C1-3-alkyl; X = N, CR5; R5 = H, Me; etc.], the tautomers thereof, the stereoisomers thereof, the mixts. thereof and the salts thereof, which have valuable pharmacol. properties, especially an inhibitory effect on the activity of the enzyme dipeptidylpeptidase-IV (DPP-IV). Thus, I·HCl [R1 = 3-aminopiperidino, R2 = 2-butynyl, R3 = (1-naphthyl)methyl, R4 = H, X = N]

was prepared from 4,5-dichloro-3-hydroxy-2H-pyridazine (II; Y1 = Y2 = Cl, Y3 = H) via N-alkylation with 1-(chloromethyl)naphthalene to give II [Y1 = Y2 = Cl, Y3 = (1-naphthyl)methyl] , hydrolysis-nitration to II [Y1 = OH, Y2 = NO2, Y3 = (1-naphthyl)methyl], amination to give II [Y1 = NH2, Y2 = NO2, Y3 = (1-naphthyl)methyl], reduction to the 4,5-diamino derivative, cyclocondensation with thiocarbonyldiimidazole to give imidazopyridazone III [Z1 = SH, Z2 = H, Z3 = (1-naphthyl)methyl], S-methylation to III [Z1 = SMe, Z2 = H, Z3 = (1-naphthyl)methyl], N-alkylation with BrCH2C.tplbond.CMe to give III [Z1 = SMe, Z2 = CH2C.tplbond.CMe, Z3 = (1-naphthyl)methyl]; S-oxidation to give III [Z1 = SO2Me, Z2 = CH2C.tplbond.CMe, Z3 = (1-naphthyl)methyl],, amination with 3-(Boc-amino)piperidine and deprotection. The inhibitory effect of I [R1 = 3-aminopiperidino, R2 = 2-butynyl, R3 = (1-naphthyl)methyl, R4 = H] on the activity of the enzyme dipeptidylpeptidase-IV (DPP-IV) was tested [IC50 = 13 nM]. Formulations containing I in the forms of dragees, tablets, ampuls, hard-gel capsules, suppositories and suspensions are presented.

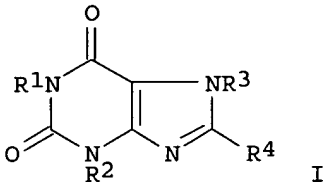
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 13 OF 34 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:450501 HCAPLUS
DOCUMENT NUMBER: 141:23542
TITLE: Preparation of xanthine derivatives as dipeptidylpeptidase IV inhibitors
INVENTOR(S): Eckhardt, Matthias; **Himmelsbach, Frank**; **Langkopf, Elke**; Maier, Roland; Mark, Michael; Tadayyon, Mohammad
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma GmbH & Co. Kg, Germany
SOURCE: Ger. Offen., 31 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10254304	A1	20040603	DE 2002-10254304	20021121
WO 2004046148	A1	20040603	WO 2003-EP12821	20031111
WO 2004046148	C1	20050714		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1565468	A1	20050824	EP 2003-782204	20031111
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CA 2506720	AA	20040603	CA 2003-2506720	20031117
US 2004138215	A1	20040715	US 2003-716141	20031118

PRIORITY APPLN. INFO.:
DE 2002-10254304 A 20021121
US 2002-432450P P 20021211
WO 2003-EP12821 W 20031111

OTHER SOURCE(S): MARPAT 141:23542
GI



I

AB Title compds. [I; R1 = ABD; A = (substituted) alkyl, etc.; B = EG; E = O, S, etc.; G = (thio)carbonyl, (imino-substituted) Me, etc.; D = propionyl, (fluorinated) alkyl, alkenyl; R2 = H, alkyl, alkenyl, alkynyl, cycloalkyl, , etc.; R3 = (substituted) alkyl, aryl, furanyl, thienyl, oxazolyl, isoxazolyl, etc.; R4 = (substituted) azetidin-1-yl, pyrrolidin-1-yl, piperidin-1-yl, etc.], were prepared Thus, 1-[(benzyloxycarbonyl)methyl]-3-methyl-7-(2-butyn-1-yl)-8[(R)-3-(tert-butyloxycarbonylamino)piperidin-1-yl]xanthine (preparation given) in CH2Cl2 was shaken with CF3CO2H for 20 min at 30° to give 97% 1-[(benzyloxycarbonyl)methyl]-3-methyl-7-(2-butyn-1-yl)-8[(R)-3-aminopiperidin-1-yl]xanthine. The latter inhibited dipeptidylpeptidase IV (DPP IV) with IC50 = 27 nM.

L22 ANSWER 14 OF 34 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:408271 HCAPLUS
DOCUMENT NUMBER: 140:423521
TITLE: Preparation of xanthines as inhibitors of dipeptidyl peptidase IV (DPP-IV)
INVENTOR(S): **Himmelsbach, Frank; Langkopf, Elke**; Eckhardt, Matthias; Maier, Roland; Mark, Michael; Tadayyon, Mohammad; Lotz, Ralf
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G., Germany
SOURCE: Ger. Offen., 39 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10251927	A1	20040519	DE 2002-10251927	20021108
US 2004138214	A1	20040715	US 2003-695597	20031028
CA 2505389	AA	20040521	CA 2003-2505389	20031103
WO 2004041820	A1	20040521	WO 2003-EP12198	20031103
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1562946	A1	20050817	EP 2003-788995	20031103
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				

PRIORITY APPLN. INFO.: DE 2002-10251927 A 20021108
US 2002-429173P P 20021126
WO 2003-EP12198 W 20031103

OTHER SOURCE(S): MARPAT 140:423521

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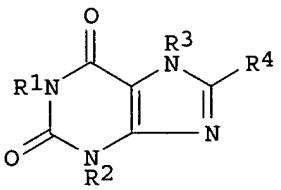

I

AB Title compds. [I; R1 = (condensed heterocyclyl-substituted) C1-3 alkyl, etc.; R2 = H, alkyl, alkenyl, alkynyl, cycloalkyl, etc.; R3 = (substituted) alkyl, aryl, alkenyl, alkynyl, etc.; R4 = (substituted) azetidin-1-yl, pyrrolidin-1-yl, piperidin-1-yl, hexahydroazepin-1-yl, etc.] and tautomerics, stereoisomerics, mixts., prodrug, and salts thereof, were prepared Thus, 1-[(1-methyl-2,2-dioxo-1H-benzo[c][1,2]thiazin-4-yl)methyl]-3-methyl-7-(3-methyl-2-buten-1-yl)-8-[3-(tert-butyloxycarbonylamino)piperidin-1-yl]xanthine (preparation given) in CH2Cl2 was treated with isopropanolic HCl followed by stirring for 3 h at room temperature to give 77% 1-[(1-methyl-2,2-dioxo-1H-benzo[c][1,2]thiazin-4-yl)methyl]-3-methyl-7-(3-methyl-2-buten-1-yl)-8-(3-aminopiperidin-1-yl)xanthine. The latter inhibited DPP-IV with IC50 = 13 nM.

L22 ANSWER 15 OF 34 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:182879 HCAPLUS
DOCUMENT NUMBER: 140:235743
TITLE: Preparation of 8-[3-aminopiperidin-1-yl]xanthines as dipeptidylpeptidase-IV (DPP-IV) inhibitors.
INVENTOR(S): **Himmelsbach, Frank; Langkopf, Elke**; Eckhardt, Matthias; Mark, Michael; Maier, Roland; Lotz, Ralf Richard Hermann; Tadayyon, Mohammad
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G., Germany
SOURCE: PCT Int. Appl., 226 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004018468	A2	20040304	WO 2003-EP9127	20030818
WO 2004018468	A3	20040408		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,

BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

DE 10238243	A1	20040304	DE 2002-10238243	20020821
DE 10312353	A1	20040930	DE 2003-10312353	20030320
CA 2496249	AA	20040304	CA 2003-2496249	20030818
EP 1532149	A2	20050525	EP 2003-792359	20030818

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

PRIORITY APPLN. INFO.:	DE 2002-10238243	A	20020821
	DE 2003-10312353	A	20030320
	WO 2003-EP9127	W	20030818

OTHER SOURCE(S): MARPAT 140:235743

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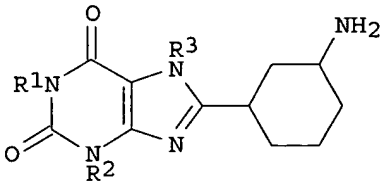

I

AB Title compds. (I; R1 = Me substituted by Me2NCO, pyrrolidin-1-ylcarbonyl, piperidin-1-ylcarbonyl, tert-butylcarbonyl, naphthyl, nitronaphthyl, dimethylaminonaphthyl, phenyloxadiazolyl, quinolinyl, indolyl, cinnolinyl, benzothienyl, etc.; R2 = Me, Me2CH, Ph; R3 = 2-methyl-2-propen-1-yl, 2-chloro-2-propen-1-yl, 3-bromo-2-propen-1-yl, 2-buten-1-yl, 2,3-dimethyl-2-buten-1-yl, 2-butyn-1-yl, 1-cyclopenten-1-ylmethyl, 2-furylmethyl), were prepared Thus, 1,3-dimethyl-7-(2,6-dicyanobenzyl)-8-bromoxanthine (preparation from 8-bromotheophylline and 2-bromomethylisophthalonitrile given), 3-aminopiperidine dihydrochloride, and K2CO3 were heated in DMF for 3 h at 80° to give 14% 1,3-dimethyl-7-(2,6-dicyanobenzyl)-8-(3-aminopiperidin-1-yl)xanthine. I inhibited DPP-IV with IC50 = 1-2160 nM.

L22 ANSWER 16 OF 34 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:	2004:177910 HCAPLUS
DOCUMENT NUMBER:	140:235734
TITLE:	Preparation of purine derivatives as dipeptidylpeptidase IV (DPP-IV) inhibitors.
INVENTOR(S):	Maier, Roland; **Himmelsbach, Frank**; Eckhardt, Matthias; **Langkopf, Elke**; Mark, Michael; Lotz, Ralf
PATENT ASSIGNEE(S):	Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G., Germany
SOURCE:	Ger. Offen., 38 pp. CODEN: GWXXBX
DOCUMENT TYPE:	Patent
LANGUAGE:	German
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10238477	A1	20040304	DE 2002-10238477	20020822
US 2004122228	A1	20040624	US 2003-634047	20030804
CA 2496211	AA	20040304	CA 2003-2496211	20030816
WO 2004018469	A1	20040304	WO 2003-EP9100	20030816

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EP 1532150	A1	20050525	EP 2003-792343		20030816
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PRIORITY APPLN. INFO.:			DE 2002-10238477	A	20020822
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			WO 2003-EP9100	W	20030816

OTHER SOURCE(S): MARPAT 140:235734
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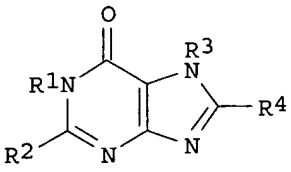

I

AB Title compds. [I; R1 = H, (substituted) alkyl, alkenyl, alkynyl, etc.; R2 = H, (substituted) alkyl, alkenyl, alkynyl, cycloalkyl, Ph, heteroaryl, etc.; R3 = (substituted) alkyl, alkenyl, alkynyl, aryl, aralkyl; R4 = substituted azetidin-1-yl, pyrrolidin-1-yl, piperidin-1-yl, hexahydroazepin-1-yl, 3-aminopiperidin-1-yl, etc.], were prepared Thus, [1-(7-benzyl-2-benzylamino-1-methyl-6-oxo-6,7-dihydro-1H-purin-8-yl)piperidin-3-yl]carbamic acid tert-Bu ester (preparation given) was stirred 2 h with CF3CO2H in CH2Cl2 to give 73.1% 8-(3-aminopiperidin-1-yl)-7-benzyl-2-benzylamino-1-methyl-1,7-dihydropurin-6-one trifluoroacetate. This inhibited DPP-IV with IC50 = 11 nM.

L22 ANSWER 17 OF 34 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:	2004:177908 HCAPLUS
DOCUMENT NUMBER:	140:235733
TITLE:	Preparation of xanthines as dipeptidylpeptidase IV inhibitors for the treatment of diabetes
INVENTOR(S):	Eckhardt, Matthias; **Himmelsbach, Frank**; **Langkopf, Elke**; Maier, Roland; Mark, Michael; Lotz, Ralf
PATENT ASSIGNEE(S):	Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G., Germany
SOURCE:	Ger. Offen., 22 pp. CODEN: GWXXBX
DOCUMENT TYPE:	Patent
LANGUAGE:	German
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10238470	A1	20040304	DE 2002-10238470	20020822

US 2004166125	A1	20040826	US 2003-636088		20030807
CA 2496325	AA	20040304	CA 2003-2496325		20030816
WO 2004018467	A2	20040304	WO 2003-EP9096		20030816
WO 2004018467	A3	20040513			

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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1554278	A2	20050720	EP 2003-792342	20030816

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PRIORITY APPLN. INFO.:	DE 2002-10238470	A	20020822
	US 2002-409258P	P	20020909
	WO 2003-EP9096	W	20030816

OTHER SOURCE(S): MARPAT 140:235733

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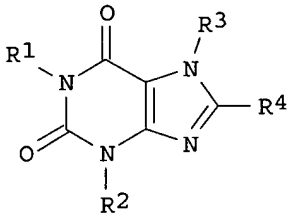

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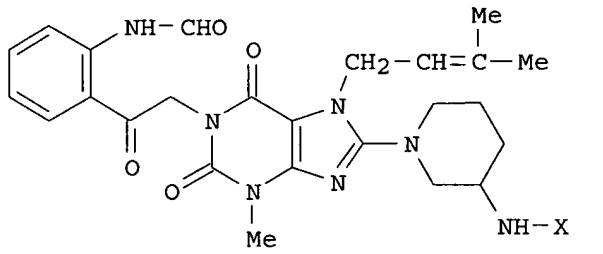

II

AB Title compds. I [R1 = (un)substituted phenylcarbonylmethyl; R2 = H, alkyl, alkenyl, etc.; R3 = (un)substituted alkyl; R4 = (un)substituted azetidin-1-yl, pyrrolidin-1-yl] and their pharmaceutically acceptable salts were prepared For example, BOC deprotection of amine II (X = Boc), e.g., prepared from 3-Methyl-8-chloroxanthine, via TFA afforded claimed xanthine II (X = H) in 87% yield. In dipeptidylpeptidase IV inhibition assays, 7-examples of compds. I exhibited IC50 values ranging from 3-11 nM, e.g., the IC50 value of xanthine II (X = H) was 5 nM. Compds. I are claimed useful for the treatment of type I and type II diabetes.

L22 ANSWER 18 OF 34 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:	2004:177895 HCAPLUS
DOCUMENT NUMBER:	140:235732
TITLE:	Production of 8-[3-aminopiperidin-1-yl]xanthines and their use as drugs
INVENTOR(S):	**Himmelsbach, Frank**; Eckhardt, Matthias; **Langkopf, Elke**; Mark, Michael; Maier, Roland; Lotz, Ralf
PATENT ASSIGNEE(S):	Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G., Germany
SOURCE:	Ger. Offen., 52 pp. CODEN: GWXXBX
DOCUMENT TYPE:	Patent

LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10238243	A1	20040304	DE 2002-10238243	20020821
US 2004097510	A1	20040520	US 2003-639036	20030812
CA 2496249	AA	20040304	CA 2003-2496249	20030818
WO 2004018468	A2	20040304	WO 2003-EP9127	20030818
WO 2004018468	A3	20040408		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1532149	A2	20050525	EP 2003-792359	20030818
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PRIORITY APPLN. INFO.:		
DE 2002-10238243	A	20020821
US 2002-409312P	P	20020909
DE 2003-10312353	A	20030320
US 2003-461752P	P	20030410
WO 2003-EP9127	W	20030818

OTHER SOURCE(S): MARPAT 140:235732
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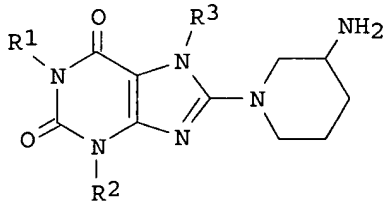

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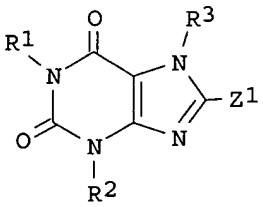

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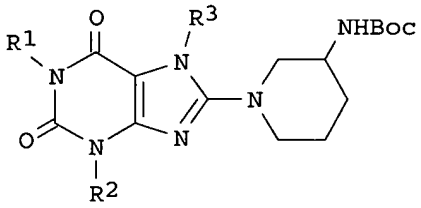

III

AB The present invention concerns substituted xanthines, e.g., I [R1 = Me, CH2CONMe2, CH2CO-(pyrrolidin-1-yl), CH2CO-(piperidin-1-yl), (un)substituted CH2-naphthyl, CH2CH:CHPh, CH2C6H4Ph, CH2-(phenyloxadiazolyl), CH2(5-methyl-3-phenylisoxazolyl), CH2(phenylpyridinyl), CH2-indolinyl, CH2-quinolinyl, CH2-isoquinolinyl,

CH2-quinazolinyl, CH2-(3,4-dihydro-4-oxophthalazinyl), CH2-(2-oxo-2H-chromenyl),CH2CH2OEt, CH2CH2OPh, CH2CH2CN, CH2COPh, CH2CH2COPh, etc.; R2 = H, Me, CHMe2, CH:CHMe, C.tplbond.CMe, Ph, CH2CN, CH2CO2Me ; R3 = CH2C2H4CN-2, CH2C2H3(CN)2-2,6, CH2CMe:CH2, CH2CCl:CH2, CH2CH:CHBr, CH2CH:CHMe, CH2CH:CMe2, CH2CMe:CMe2, CH2C.tplbond.CMe, (1-cyclopenten-1-yl)methyl, 2-furanylmethyl] their tautomers, their stereoisomers, their mixts., their prodrugs and their salts, which contain valuable pharmacol. properties, in particular an inhibiting effect on the activity of the enzyme dipeptidylpeptidase IV (DPP-IV). The procedure for the preparation of I is characterized by, reaction of xanthine II [Z1 = leaving group, e.g. halogen, substituted OH, SH, sulfinyl, sulfonyl, sulfonyloxy] with 3-aminopiperidine, its enantiomers, or their salts or its preparation via piperidine derivative III (Boc = CO2CMe3). Thus, 1-[(quinazolin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-[(R)-3-aminopiperidin-1-yl]xanthine [(R)-I; R1 = (quinazolin-2-yl)methyl, R2 = Me, R3 = CH2C.tplbond.CMe] was prepared from III [R1 = (quinazolin-2-yl)methyl, R2 = Me, R3 = CH2C.tplbond.CMe] via deprotection with CF3CO2H in CH2Cl2. The inhibiting effect of (R)-I [R1 = (quinazolin-2-yl)methyl, R2 = Me, R3 = CH2C.tplbond.CMe] on the activity of the enzyme dipeptidylpeptidase IV was determined [IC50 = 1 nM].

L22 ANSWER 19 OF 34 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:796492 HCAPLUS
DOCUMENT NUMBER: 139:307786
TITLE: Preparation of 4-(phenylamino)quinazolines as inhibitors of EGF-receptor kinase
INVENTOR(S): **Himmelsbach, Frank; Jung, Birgit;** Solca, Flavio
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G., Germany
SOURCE: PCT Int. Appl., 148 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003082290	A1	20031009	WO 2003-EP3062	20030325
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
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DE 10231711	A1	20040122	DE 2002-10231711	20020713
CA 2476008	AA	20031009	CA 2003-2476008	20030325
BR 2003008902	A	20050104	BR 2003-8902	20030325
EP 1492536	A1	20050105	EP 2003-745271	20030325
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PRIORITY APPLN. INFO.:
DE 2002-10214412 A 20020330
DE 2002-10231711 A 20020713
WO 2003-EP3062 W 20030325
OTHER SOURCE(S): MARPAT 139:307786

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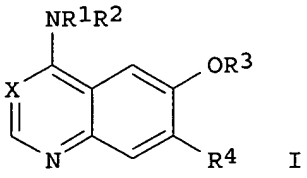

I

AB Title compds. [I; R1 = H, C1-4 alkyl; R2 = (substituted) Ph, 1-phenylethyl; R3 = (amino-substituted) cyclobutyl, cyclopentyl, cyclohexyl; R4 = H, F, Cl, Br, alkoxy, (fluorinated) OMe, OCH2CH3, (substituted) alkyloxy, etc.; X = N, cyano-substituted CH], tautomers, stereoisomers, mixts., and salts thereof, especially the physiol. acceptable salts thereof with organic and inorg. acids, were prepared Thus, 4-[(3-chloro-4-fluorophenyl)amino]-6-hydroxy-7-methoxyquinazoline in MeCN was treated with (R)-3-hydroxytetrahydrofuran and Ph3P followed by stirring with di-Et azodiformate over night at room temperature to give 15% 4-[(3-chloro-4-fluorophenyl)amino]-6-((S)-tetrahydrofuran-3-yloxy)-7-methoxyquinazoline. The latter inhibited EGF-receptor kinase with IC50 = 0.13 nM.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 20 OF 34 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:793441 HCAPLUS
DOCUMENT NUMBER: 139:292268
TITLE: Preparation of bicyclic heterocycles especially quinazolines as inhibitors of EGF-receptor kinase
INVENTOR(S): **Himmelsbach, Frank; Jung, Birgit;** Solca, Flavio
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma GmbH & Co. KG, Germany
SOURCE: Ger. Offen., 38 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10214412	A1	20031009	DE 2002-10214412	20020330
CA 2476008	AA	20031009	CA 2003-2476008	20030325
WO 2003082290	A1	20031009	WO 2003-EP3062	20030325
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EP 1492536	A1	20050105	EP 2003-745271	20030325
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	US 2004048880		A1	20040311		US 2003-400370							20030327
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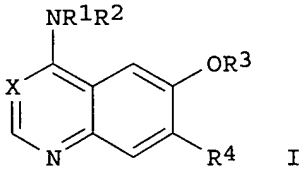
OTHER SOURCE(S): MARPAT 139:292268

GI



I

AB Title compds. [I; R1 = H, C1-4 alkyl; R2 = (substituted) Ph, 1-phenylethyl; R3 = (amino-substituted) cyclobutyl, cyclopentyl, cyclohexyl; R4 = H, F, Cl, Br, alkoxy, (fluorinated) OMe, OCH2CH3, (substituted) alkyloxy, etc.; X = N, cyano-substituted CH], tautomers, stereoisomers, and salts thereof, especially the physiol. acceptable salts thereof with inorg. or organic acids, were prepared Thus, 4-[(3-chloro-4-fluorophenyl)amino]-6-hydroxy-7-methoxyquinazoline in MeCN was treated with (R)-3-hydroxytetrahydrofuran and Ph3P followed by stirring with di-Et azodiformate over night at room temperature to give 15% 4-[(3-chloro-4-fluorophenyl)amino]-6-((S)-tetrahydrofuran-3-yloxy)-7-methoxyquinazoline. The latter inhibited EGF-receptor kinase with IC50 = 0.13 nM.

L22 ANSWER 21 OF 34 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:	2002:676018 HCAPLUS
DOCUMENT NUMBER:	137:216824
TITLE:	Preparation of xanthine derivatives as dipeptidylpeptidase-IV inhibitors
INVENTOR(S):	**Himmelsbach, Frank**; Mark, Michael; Eckhardt, Matthias; **Langkopf, Elke**; Maier, Roland; Lotz, Ralf
PATENT ASSIGNEE(S):	Boehringer Ingelheim Pharma K.-G., Germany
SOURCE:	PCT Int. Appl., 373 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	German
FAMILY ACC. NUM. COUNT:	2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002068420	A1	20020906	WO 2002-EP1820	20020221
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,				

	CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10109021	A1	20020905	DE 2001-10109021		20010224
DE 10117803	A1	20021024	DE 2001-10117803		20010410
DE 10140345	A1	20030227	DE 2001-10140345		20010817
DE 10203486	A1	20030731	DE 2002-10203486		20020130
CA 2435730	AA	20020906	CA 2002-2435730		20020221
EP 1368349	A1	20031210	EP 2002-701288		20020221
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
EE 200300409	A	20031215	EE 2003-409		20020221
BR 2002007767	A	20040330	BR 2002-7767		20020221
JP 2004522786	T2	20040729	JP 2002-567932		20020221
BG 108093	A	20040831	BG 2003-108093		20030813
NO 2003003726	A	20030821	NO 2003-3726		20030821
US 2004077645	A1	20040422	US 2003-467961		20031205
PRIORITY APPLN. INFO.:			DE 2001-10109021	A	20010224
			DE 2001-10117803	A	20010410
			DE 2001-10140345	A	20010817
			DE 2002-10203486	A	20020130
			WO 2002-EP1820	W	20020221

OTHER SOURCE(S): MARPAT 137:216824

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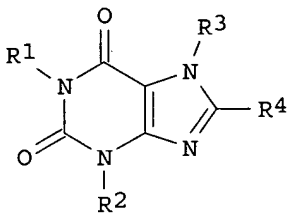

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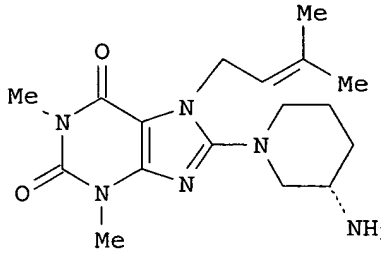

II

AB Xanthine derivs. of formula I [R1, R2 = H, alkyl, alkenyl, etc.; R3 = alkyl, arylalkyl, etc.; R4 = heterocyclyl, cycloalkyl, aminoalkyl, etc.] are prepared which exhibit an inhibitory effect on the activity of the dipeptidylpeptidase-IV enzyme. Pharmaceutical compns. containing I are described. Thus, II was prepared and had an IC50 of 22 nM against dipeptidylpeptidase-IV.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 22 OF 34 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:171891 HCAPLUS

DOCUMENT NUMBER: 136:216761

TITLE: Preparation of 4-amino-6-vinylcarbonylaminoquinazolines as epidermal growth factor receptor signal transduction inhibitors

INVENTOR(S): **Himmelsbach, Frank**; **Langkopf, Elke**; **Jung, Birgit**; Blech, Stefan; Solca, Flavio

PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma Kg, Germany

SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002018375	A1	20020307	WO 2001-EP9534	20010818
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10042064	A1	20020307	DE 2000-10042064	20000826
AU 2002010444	A5	20020313	AU 2002-10444	20010818
CA 2417955	AA	20030130	CA 2001-2417955	20010818
EP 1322645	A2	20030702	EP 2001-978279	20010818
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004507537	T2	20040311	JP 2002-523890	20010818
US 6403580	B1	20020611	US 2001-935498	20010823

PRIORITY APPLN. INFO.:		DE 2000-10042064	A	20000826
		US 2000-230541P	P	20000905
		WO 2001-EP9534	W	20010818

OTHER SOURCE(S): MARPAT 136:216761

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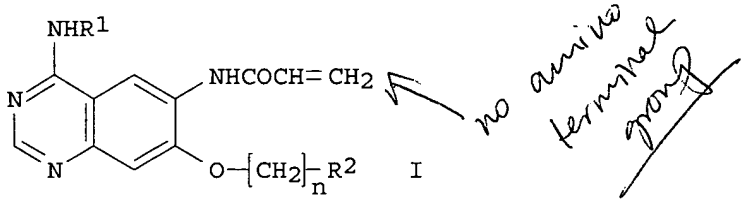

AB Title compds. [I; R1 = PhCH2, 1-phenylethyl, (substituted) Ph; R2 = N-(2-oxotetrahydrofuran-4-yl)methylamino, N(CH2CO2R3)2, (substituted) R4OCOCH2NCH2CH2OH, 2-oxomorpholin-4-yl; R3 = H, Me, Et; R4 = H, alkyl; n = 2-4],were prepared Thus, a mixture of CH2:CHCO2H and Et3N was stirred for 1 h at -50° with CH2:CHCO2Cl in THF followed by addition of 6-amino-4-[(3-chloro-4-fluorophenyl)amino]-7-[3-(2,2-dimethyl-6-oxomorpholin-4-yl)propyloxy]quinazoline (preparation given) in THF at -55° and slowly heating up at 0° up to completely conversion to give 60% 4-[(3-chloro-4-fluorophenyl)amino]-7-[3-(2,2-dimethyl-6-oxomorpholin-4-yl)propyloxy]-6-[(vinylcarbonyl)amino]quinazoline. One of the exemplified examples, 4-[(R)-(1-phenylethyl)amino]-7-[2-(2,2-dimethyl-6-oxomorpholin-4-yl)ethoxy]-6-[(vinylcarbonyl)amino]quinazoline, inhibited epidermal growth factor (EGF)-dependent proliferation of F/L-HERc cells with IC50 = 0.4 nM. The invention relates to the use of the title compds. for treating tumor diseases, and lung and respiratory tract disorders.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 23 OF 34 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:171888 HCAPLUS
DOCUMENT NUMBER: 136:216759

TITLE: Preparation of aminoquinazolines as epidermal growth factor receptor signal transduction inhibitors

INVENTOR(S): **Himmelsbach, Frank**; **Langkopf, Elke**; **Jung, Birgit**; Blech, Stefan; Solca, Flavio

PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma Kg, Germany

SOURCE: PCT Int. Appl., 95 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002018372	A1	20020307	WO 2001-EP9533	20010818
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10042059	A1	20020307	DE 2000-10042059	20000826
AU 2001095481	A5	20020313	AU 2001-95481	20010818
CA 2417652	AA	20030128	CA 2001-2417652	20010818
EP 1315718	A1	20030604	EP 2001-976107	20010818
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004507535	T2	20040311	JP 2002-523887	20010818
US 2002049197	A1	20020425	US 2001-938314	20010823
US 6617329	B2	20030909		

PRIORITY APPLN. INFO.:

DE 2000-10042059	A	20000826
US 2000-230118P	P	20000905
WO 2001-EP9533	W	20010818

OTHER SOURCE(S): MARPAT 136:216759

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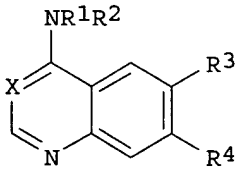

I

AB Title compds. [I; X = N, (substituted) methynyl; R1 = H, Me; R2 = (substituted) Ph, PhCH2, 1-phenylethyl; R3, R4 = AB, CD; A = (oxy)alkenyl, O; B = (substituted) pyrrolidinyl, piperidinyl, hexahydroazepinyl, piperazinyl, 2-oxomorpholin-4-yl, etc.; C = oxyalkenyl, O; D = (substituted) amino, alkenylimino, imidazolyl, heterocycloalkyl, alkoxy, cycloalkoxy, cycloalkylalkoxy, tetrahydrofuran-3-yloxy, tetrahydropyran-3-yloxy, tetrahydropyran-4-yloxy, tetrahydrofuranylmethoxy, tetrahydropyranylmethoxy, etc.; or CD = H], were prepared Thus, 4-[(3-chloro-4-fluorophenyl)amino]-6-cyclopentyloxy-7-[2-

(piperazin-1-yl)ethoxy]quinazoline (preparation given) in MeCN was refluxed for 4 h with K2CO3, NaI, and (R)-5-[(methanesulfonyloxy)methyl]-2-oxotetrahydrofuran followed by addition of (R)-5-[(methanesulfonyloxy)methyl]-2-oxotetrahydrofuran and reflux for 15 h to give 47% 4-[(3-chloro-4-fluorophenyl)amino]-6-cyclopentyloxy-7-[2-(4-[(R)-(2-oxotetrahydrofuran-5-yl)methyl]piperazin-1-yl)ethoxy]quinazoline. Several I inhibited epidermal growth factor (EGF)-dependent proliferation of F/L-HERc cells with IC50 = 4-67 nM. The invention relates to the use of the title compds. for treating tumor diseases, and lung and respiratory tract disorders.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 24 OF 34 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:171886 HCAPLUS
DOCUMENT NUMBER: 136:216758
TITLE: Preparation of 4-amino-6-heterocyclylcarbonylaminoquinazolines as epidermal growth factor receptor signal transduction inhibitors
INVENTOR(S): **Himmelsbach, Frank**; **Langkopf, Elke**; **Jung, Birgit**; Blech, Stefan; Solca, Flavio
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma Kg, Germany
SOURCE: PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002018370	A1	20020307	WO 2001-EP9535	20010818
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10042061	A1	20020307	DE 2000-10042061	20000826
CA 2417042	AA	20020307	CA 2001-2417042	20010818
AU 2001089814	A5	20020313	AU 2001-89814	20010818
EP 1315716	A1	20030604	EP 2001-969610	20010818
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004507533	T2	20040311	JP 2002-523885	20010818
US 2002082270	A1	20020627	US 2001-934753	20010822

PRIORITY APPLN. INFO.:	DE 2000-10042061	A	20000826
	US 2000-230119P	P	20000905
	WO 2001-EP9535	W	20010818

OTHER SOURCE(S): MARPAT 136:216758
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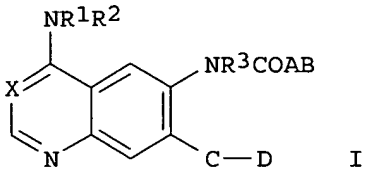

I

AB Title compds. [I; X = N, (substituted) methynyl; R1 = H, Me; R2 = (substituted) Ph, PhCH2, 1-phenylethyl; R3 = H, Me; A = (substituted) vinyl, ethynyl, 1,3-butadien-1,4-yl; B = H, (substituted) alkyl, alkylcarbonyl, CO2H, alkoxycarbonyl, aminocarbonyl, (di)alkylaminocarbonyl, pyrrolidinylcarbonyl, piperidinylcarbonyl, morpholinocarbonyl, alkylpiperazinylcarbonyl; C = (oxy)alkenyl, O; D = (substituted) pyrrolidinyl, piperidinyl, hexahydroazepinyl, piperazinyl, etc.], were prepared Thus, a mixture of CH2:CHCO2H and Et3N was stirred for 45 min at -50° with CH2:CHCO2Cl in THF followed by dropwise addition of 6-amino-4-[(3-chloro-4-fluorophenyl)amino]-7-(3-[4-(2-oxotetrahydrofuran-4-yl)piperazin-1-yl]propyloxy)quinazoline (preparation given) in THF for 20 min and stirring at 0° up to completely conversion to give 31% 4-[(3-chloro-4-fluorophenyl)amino]-7-(3-[4-(2-oxotetrahydrofuran-4-yl)piperazin-1-yl]propyloxy)-6-[(vinylcarbonyl)amino]quinazoline. The latter inhibited epidermal growth factor (EGF)-dependent proliferation of F/L-HERc cells with IC50 = 12 nM. The invention relates to the use of the title compds. for treating tumor diseases, and lung and respiratory tract disorders.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 25 OF 34 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:171867 HCAPLUS
DOCUMENT NUMBER: 136:232314
TITLE: Preparation of aminoquinazolines as epidermal growth factor receptor signal transduction inhibitors
INVENTOR(S): **Himmelsbach, Frank**; **Langkopf, Elke**; **Jung, Birgit**; Blech, Stefan; Solca, Flavio
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma Kg, Germany
SOURCE: PCT Int. Appl., 103 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002018351	A1	20020307	WO 2001-EP9532	20010818
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10042058	A1	20020307	DE 2000-10042058	20000826
AU 2001087694	A5	20020313	AU 2001-87694	20010818

CA 2417897	AA	20030130	CA 2001-2417897		20010818
EP 1315705	A1	20030604	EP 2001-967285		20010818
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
BR 2001013519	A	20030701	BR 2001-13519		20010818
JP 2004507529	T2	20040311	JP 2002-523469		20010818
EE 200300077	A	20041215	EE 2003-77		20010818
US 2002082271	A1	20020627	US 2001-934772		20010822
US 6656946	B2	20031202			
ZA 2003000991	A	20040416	ZA 2003-991		20030205
BG 107559	A	20031031	BG 2003-107559		20030214
NO 2003000870	A	20030225	NO 2003-870		20030225
PRIORITY APPLN. INFO.:			DE 2000-10042058	A	20000826
			US 2000-230035P	P	20000905
			WO 2001-EP9532	W	20010818

OTHER SOURCE(S): MARPAT 136:232314

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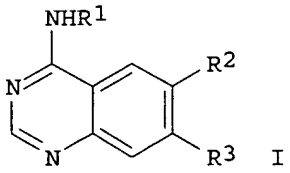


I

AB Title compds. [I; R1 = PhCH2, 1-phenylethyl, (substituted) Ph; R2, R3 = O(CH2)mR4, methoxy, cyclobutyloxy, cyclopentyloxy, cyclopropylmethoxy, cyclobutylmethoxy, cyclopentylmethoxy, tetrahydrofuran-3-yloxy, tetrahydropyran-3-yloxy, tetrahydropyran-4-yloxy, tetrahydrofuranylmethoxy, tetrahydropyranylmethoxy; R4 = N-(2-oxotetrahydrofuran-4-yl)methylamino, N-(2-oxotetrahydrofuran-4-yl)ethylamino, (substituted) 2-oxo-morpholin-4-yl, R5OCOCH2NCH2CH2OH; R5 = H, alkyl; m = 2-4], were prepared Thus, 4-[(3-bromophenyl)amino]-6-[2-(N-[(tert-butyloxycarbonyl)methyl]-N-((S)-2-hydroxypropyl)amino)ethoxy]-7-methoxyquinazoline (preparation given) in MeCN was stirred under reflux with MeSO2OH for 3 h followed by addition of MeSO2OH up to completely conversion to give 85% 4-[(3-bromophenyl)amino]-6-[2-((S)-6-methyl-2-oxomorpholin-4-yl)ethoxy]-7-methoxyquinoline. Tested I inhibited epidermal growth factor (EGF)-dependent proliferation of F/L-HERc cells with IC50 = 29-59 nM. The invention relates to the use of the title compds. for treating tumor diseases, and lung and respiratory tract disorders.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 26 OF 34 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:666735 HCAPLUS

DOCUMENT NUMBER: 133:238019

TITLE: Preparation of aminopyrimidopyrimidines and related compounds as inhibitors of epidermal growth factor receptor-mediated cell proliferation.

INVENTOR(S): **Himmelsbach, Frank**; **Langkopf, Elke**; Blech, Stefan; **Jung, Birgit**; **Metz, Thomas**; Solca, Flavio

PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany

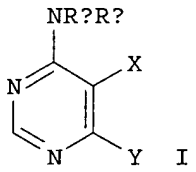
SOURCE: PCT Int. Appl., 137 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000055162	A2	20000921	WO 2000-EP2229	20000314
WO 2000055162	A3	20001228		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19911510	A1	20000921	DE 1999-19911510	19990315
CA 2361770	AA	20000921	CA 2000-2361770	20000314
EP 1163242	A2	20011219	EP 2000-920498	20000314
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002539214	T2	20021119	JP 2000-605591	20000314
US 2002082420	A1	20020627	US 2001-933597	20010821
PRIORITY APPLN. INFO.:			DE 1999-19911510 A	19990315
			WO 2000-EP2229 W	20000314

OTHER SOURCE(S): MARPAT 133:238019
GI



I

AB Title compds. [I; Ra = H, alkyl; Rb = (substituted) Ph, PhCH2, PhCH2CH2; XY = N:C(AB)CH:CH, CH:NC(AB):CH, N:C(AB)N:CH, etc.; A = alkyleneoxy, cycloalkyleneoxy, (substituted) alkyleneimino, cycloalkyleneimino, azetidinylene, piperidinylene, piperazinylene, etc.; B = R6O2CA1NR5, etc.; R5 = H, (substituted) alkyl, cycloalkyl, cycloalkylalkyl; A1 = (substituted) alkylene; R6 = H, (substituted) alkyl, cycloalkyl, alkenyl, alkynyl, cycloalkylalkyl, etc.], were prepared Thus, 4-[(3-chloro-4-fluorophenyl)amino]-6-[[1-[(methoxycarbonyl)methyl]piperidin-4-yl]amino]pyrimido[5,4-d]pyrimidine was stirred with aqueous NaOH in THF to give 96% 4-[(3-chloro-4-fluorophenyl)amino]-6-[[1-[(carboxymethyl)methyl]piperidin-4-yl]amino]pyrimido[5,4-d]pyrimidine. I inhibited EGF-dependent proliferation of F/L-HERc cells with IC50 = 7-2510 nM.

L22 ANSWER 27 OF 34 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:666715 HCAPLUS
DOCUMENT NUMBER: 133:252449
TITLE: Quinazolines and other bicyclic heterocycles, pharmaceutical compositions containing these compounds as tyrosine kinase inhibitors, and processes for preparing them

INVENTOR(S): **Himmelsbach, Frank**; **Langkopf, Elke** ; Blech, Stefan; **Jung, Birgit**; **Metz, Thomas**; Solca, Flavio
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany
SOURCE: PCT Int. Appl., 153 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000055141	A1	20000921	WO 2000-EP2228	20000314
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19911509	A1	20000921	DE 1999-19911509	19990315
CA 2368059	AA	20000921	CA 2000-2368059	20000314
EP 1163227	A1	20011219	EP 2000-909360	20000314
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000009076	A	20011226	BR 2000-9076	20000314
TR 200102782	T2	20020422	TR 2001-200102782	20000314
JP 2002539199	T2	20021119	JP 2000-605571	20000314
EE 200100484	A	20021216	EE 2001-484	20000314
NZ 514706	A	20031128	NZ 2000-514706	20000314
AU 772520	B2	20040429	AU 2000-31667	20000314
US 2002177601	A1	20021128	US 2001-938235	20010823
ZA 2001007185	A	20020621	ZA 2001-7185	20010830
BG 105893	A	20020531	BG 2001-105893	20010912
NO 2001004487	A	20010914	NO 2001-4487	20010914
HK 1043124	A1	20041203	HK 2002-104697	20020625

PRIORITY APPLN. INFO.: DE 1999-19911509 A 19990315
WO 2000-EP2228 W 20000314

OTHER SOURCE(S): MARPAT 133:252449
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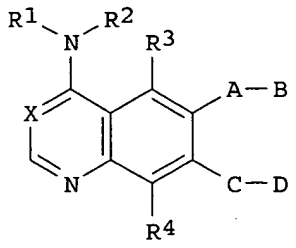

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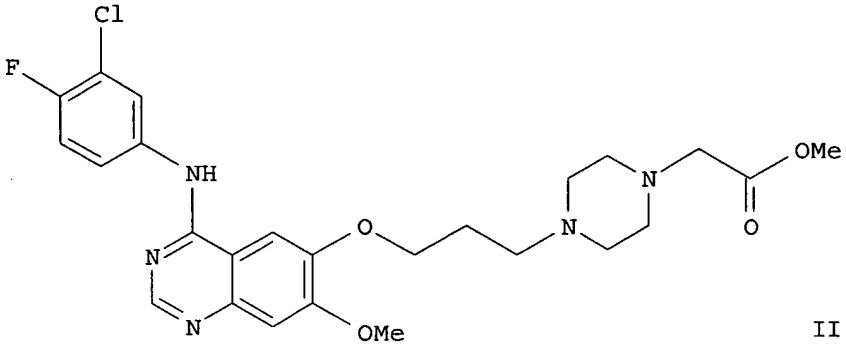


II

AB The invention relates to bicyclic heterocyclic compds. I [R1 = H, alkyl; R2 = (un)substituted Ph, CH2Ph, or CH(Me)Ph; R3, R4 = H, F, Cl, OMe, or Me optionally substituted by OMe, NMe2, NEt2, pyrrolidino, piperidino, or morpholino; X = N or C(CN); A = O, NH, (un)substituted alkylene, O-alkylene, NH-alkylene, O-cycloalkylene, etc.; B = (un)substituted amine-containing sidechain, piperazino, alkyleneimino, morpholino, etc.; or AB = H, F, Cl, alkoxy, amino, etc.; C = groups similar to A; D = groups similar to B; with a variety of provisos] and their tautomers, stereoisomers, and salts, and particularly their physiol. acceptable salts with inorg. or organic acids or bases. The compds. have valuable pharmacol. properties, particularly an inhibitory effect on signal transduction mediated by tyrosine kinases, and are useful in treating diseases, particularly tumor diseases, and diseases of the lung and airways. Over 20 compds. were prepared, and over 200 are listed. For instance, alkylation of 4-(3-chloro-4-fluorophenylamino)-6-[3-(1-piperazinyl)propyloxy]-7-methoxyquinazoline (preparation given) by Me bromoacetate gave 51% title compound
II. The latter compound inhibited EGF-dependent proliferation of F/L-HERc cells in vitro, with an IC50 of 46 nM.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 28 OF 34 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:228536 HCAPLUS
DOCUMENT NUMBER: 133:26567
TITLE: A comparative cell-based high throughput screening strategy for the discovery of selective tyrosine kinase inhibitors with anticancer activity
AUTHOR(S): Stratowa, Christian; **Baum, Anke**; Castanon, Maria J.; Dahmann, Georg; **Himmelsbach, Frank**; Himmler, Adolf; Loeber, Gerhard; **Metz, Thomas**; Schnitzer, Renate; Solca, Flavio; Spevak, Walter; Tontsch, Ulrike; Von Ruden, Thomas
CORPORATE SOURCE: Boehringer Ingelheim Austria GmbH, Research and Development, Vienna, A-1121, Austria

SOURCE: Anti-Cancer Drug Design (1999), 14(5), 393-402
CODEN: ACDDEA; ISSN: 0266-9536
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Growth factor receptor tyrosine kinases (RTK) have been implicated in tumor growth, metastasis and angiogenesis, and are thus considered promising targets for therapeutic intervention in malignant diseases. We present a novel drug discovery strategy to find inhibitors of RTKs based on comparative screening of compound libraries employing functional cellular assays. Cell lines stably expressing HER2 and the receptors for hepatocyte growth factor (HGF), vascular endothelial growth factor (VEGF), insulin-like growth factor-I (IGF-I) and epidermal growth factor (EGF) have been established. All cell lines are based on FDC-P1, a murine myeloid progenitor cell line which allows a direct comparison of results obtained in primary screens. In addition, the same cell lines are suitable for compound optimization and for animal studies. Using this strategy we report the identification of promising lead candidates for further drug development which are highly selective, non-cytotoxic and cell permeable with potencies in the low micromolar range.

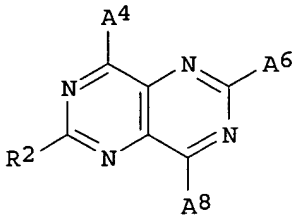
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 29 OF 34 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:618102 HCAPLUS
DOCUMENT NUMBER: 127:278208
TITLE: Preparation of pyrimido[5,4-d]pyrimidines as tyrosine kinase signal transduction inhibitors
INVENTOR(S): **Himmelsbach, Frank**; Dahmann, Georg; Von Ruden, Thomas; **Metz, Thomas**
PATENT ASSIGNEE(S): Dr. Karl Thomae G.m.b.H., Germany
SOURCE: PCT Int. Appl., 151 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9732882	A1	19970912	WO 1997-EP1058	19970303
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
DE 19608653	A1	19970911	DE 1996-19608653	19960306
CA 2248316	AA	19970912	CA 1997-2248316	19970303
AU 9719252	A1	19970922	AU 1997-19252	19970303
AU 712072	B2	19991028		
EP 885227	A1	19981223	EP 1997-907067	19970303
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI				
CN 1212696	A	19990331	CN 1997-192789	19970303
BR 9708004	A	19990727	BR 1997-8004	19970303
JP 2000506153	T2	20000523	JP 1997-531445	19970303
ZA 9701886	A	19980907	ZA 1997-1886	19970305

US 5977102	A	19991102	US 1997-812002		19970305
NO 9804081	A	19980904	NO 1998-4081		19980904
PRIORITY APPLN. INFO.:			DE 1996-19608653	A	19960306
			WO 1997-EP1058	W	19970303

OTHER SOURCE(S): MARPAT 127:278208
GI



I

AB Title compds. [I; A2,A8 = H or alkyl; A4 = NRaRb or NRdRe; A6 = Rc or Rg; Ra,Rd = H or alkyl; Rb = (un)substituted Ph; Rc = azetidino, (un)substituted pyrrolidino, -piperidino, etc.; Re = 2-fluorenyl, (un)substituted phenylalkyl, heteroaryl, etc.; Rg = alkyl, (spiro)alkyleneimino, (di)(alkyl)amino, etc.] were prepared Thus, 5-bromo-2-methylthiopyrimidine-4-carboxylic acid was aminated and the product cyclocondensed with HCONH2 to give I (A2 = A8 = H)(II; A4 = OH, A6 = SMe) which was converted in 4 steps to II (A4 = 5-indolylamino, A6 = morpholino). Data for biochem. activity of I were given.

L22 ANSWER 30 OF 34 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:618101 HCAPLUS
DOCUMENT NUMBER: 127:278207
TITLE: Preparation of 4-aminopyrimidine derivatives as antitumor agents.
INVENTOR(S): **Himmelsbach, Frank**; Dahmann, Georg; Von Ruden, Thomas; **Metz, Thomas**
PATENT ASSIGNEE(S): Dr. Karl Thomae G.m.b.H., Germany; Himmelsbach, Frank; Dahmann, Georg; Von Ruden, Thomas; Metz, Thomas
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9732881	A1	19970912	WO 1997-EP1057	19970303
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
DE 19608631	A1	19970911	DE 1996-19608631	19960306
DE 19629652	A1	19980129	DE 1996-19629652	19960723
CA 2243994	AA	19970912	CA 1997-2243994	19970303
AU 9719251	A1	19970922	AU 1997-19251	19970303

AU 710274		B2	19990916			
EP 885226		A1	19981223	EP 1997-907066		19970303
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI						
CN 1212695		A	19990331	CN 1997-192787		19970303
BR 9708312		A	19990803	BR 1997-8312		19970303
NZ 331546		A	20000327	NZ 1997-331546		19970303
JP 2000506847		T2	20000606	JP 1997-531444		19970303
NO 9804084		A	19980904	NO 1998-4084		19980904
PRIORITY APPLN. INFO.:				DE 1996-19608631	A	19960306
				DE 1996-19629652	A	19960723
				WO 1997-EP1057	W	19970303

OTHER SOURCE(S): MARPAT 127:278207
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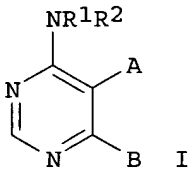

I

AB Title compds. [I; R1 = H, Me; R2 = (substituted) Ph, phenylalkyl; AB = NCR3CH:CH, CH:NCR3CH, etc.; R3 = (substituted) morpholino, piperazinyl, oxopiperazinyl, azetidinyl, pyrrolidinyl, piperidinyl, azacycloheptyl], were prepared Thus, 4-[(3-chloro-4-fluorophenyl)amino]-7-(4-amino-1-piperidinyl)pyrido[4,3-d]pyrimidine (preparation given) was heated with 4-aminopyrimidine in Me2CHOH to give 4-[(3-chloro-4-fluorophenyl)amino]-7-(4-amino-1-piperidinyl)pyrido[4,3-d]pyrimidine. I inhibited epidermal growth factor-induced cell proliferation with IC50 = 0.001-0.30 μM.

L22 ANSWER 31 OF 34 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:618100 HCAPLUS
DOCUMENT NUMBER: 127:278206
TITLE: Preparation of pyrimido[5,4-d]pyrimidines as tyrosine kinase signal transduction inhibitors
INVENTOR(S): **Himmelsbach, Frank**; Dahmann, Georg; Von Ruden, Thomas; **Metz, Thomas**
PATENT ASSIGNEE(S): Dr. Karl Thomae G.m.b.H., Germany
SOURCE: PCT Int. Appl., 159 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9732880	A1	19970912	WO 1997-EP1047	19970303
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				

DE 19608588	A1	19970911	DE 1996-19608588	19960306
CA 2248720	AA	19970912	CA 1997-2248720	19970303
AU 9720945	A1	19970922	AU 1997-20945	19970303
AU 730376	B2	20010308		
EP 888351	A1	19990107	EP 1997-906152	19970303
EP 888351	B1	20031015		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI				
CN 1212694	A	19990331	CN 1997-192784	19970303
CN 1064362	B	20010411		
BR 9707839	A	19990727	BR 1997-7839	19970303
NZ 331545	A	20000327	NZ 1997-331545	19970303
JP 2000506151	T2	20000523	JP 1997-531440	19970303
RU 2195461	C2	20021227	RU 1998-118380	19970303
AT 252101	E	20031115	AT 1997-906152	19970303
ZA 9701887	A	19980907	ZA 1997-1887	19970305
US 5821240	A	19981013	US 1997-811907	19970305
TW 454008	B	20010911	TW 1997-86102755	19970306
NO 9804082	A	19980904	NO 1998-4082	19980904
NO 311522	B1	20011203		
BG 63163	B1	20010531	BG 1998-102789	19980924
HK 1018450	A1	20010713	HK 1999-103458	19990810

PRIORITY APPLN. INFO.: DE 1996-19608588 A 19960306
WO 1997-EP1047 W 19970303

OTHER SOURCE(S): MARPAT 127:278206

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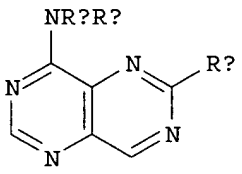

I

AB Title compds. [I; Ra = H; Rb = (un)substituted Ph; NRaRb = 1-indolinyl or 1,2,3,4-tetrahydroquinol-1-yl; Rc = substituted pyrrolidino, -piperidino, 4-piperidinyloxy, NR4R5, etc.; R4 = H or alkyl; R5 = H, cycloalkyl(methyl), substituted Ph, etc.] were prepared Thus, 5-bromo-2-methylthiopyrimidine-4-carboxylic acid was aminated and the product cyclocondensed with HCONH2 to give 4-hydroxy-6-methylthiopyrimido[5,4-d]pyrimidine which was converted in 4 steps to I (Ra = H, Rb = 3-chloro-4-fluorophenyl, Rc = 4-methoxycarbonylcyclohexylamino). Data for biol. activity of I were given.

L22 ANSWER 32 OF 34 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:721779 HCAPLUS
DOCUMENT NUMBER: 126:8131
TITLE: Preparation of 4-aminoimidazo[5,4-g]quinazolines as inhibitors of tyrosine kinase-mediated signal transduction.
INVENTOR(S): **Himmelsbach, Frank**; Dahmann, Georg; Von, Rueden Thomas; **Metz, Thomas**
PATENT ASSIGNEE(S): Karl Thomae Gmbh, Germany
SOURCE: PCT Int. Appl., 73 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German

FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9629331	A1	19960926	WO 1996-EP1082	19960314
W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
DE 19510019	A1	19960926	DE 1995-19510019	19950320
DE 19600785	A1	19970717	DE 1996-19600785	19960111
AU 9651081	A1	19961008	AU 1996-51081	19960314
PRIORITY APPLN. INFO.:			DE 1995-19510019 A	19950320
			DE 1996-19600785 A	19960111
			WO 1996-EP1082 W	19960314

OTHER SOURCE(S): MARPAT 126:8131
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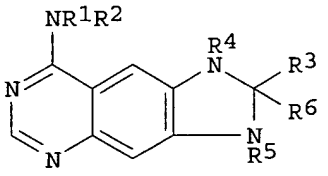

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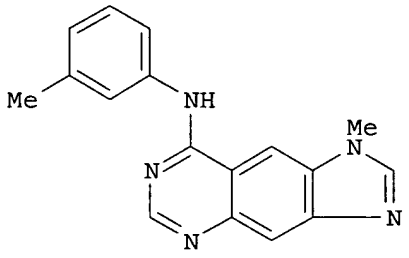


II

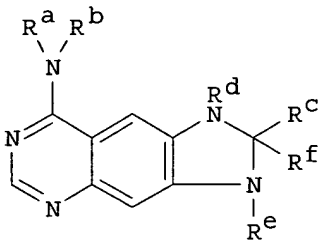
AB Title compds. [I; R1 = H, Me; R2 = 2-naphthyl, 1,2,3,4-tetrahydro-6-naphthyl, 5-indanyl, (substituted) Ph; R3 = H, OH, SH, Cl, amino, CO2H, (substituted) alkyl, alkoxy, aminocarbonyl, morpholino, pyrrolidinyl, benzoylamino, tetrahydrofuryl, aryl, etc.; R4 = (substituted) alkyl, cycloalkyl, alkenyl, alkynyl; R5R6 = bond; R3R4 or R3R5 = (alkyl-substituted) (heteroatom-interrupted) alkylene; R4R6, R5R6 = bond], were prepared Thus, 6-methyl-4-methylthioimidazo[5,4-g]quinazoline (preparation given) and m-toluidine were heated at 170° for 2 h to give title compound (II). II inhibited EGF-dependent proliferation of F/L-HERc cells with IC50 = 0.02 μM.

L22 ANSWER 33 OF 34 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:625525 HCAPLUS
DOCUMENT NUMBER: 125:275902
TITLE: Imidazo[4,5-g]quinazolines, pharmaceuticals containing them, their use as antitumor agents, and process for their preparation.
INVENTOR(S): **Himmelsbach, Frank**; Dahmann, Georg; Von Rueden, Thomas; **Metz, Thomas**
PATENT ASSIGNEE(S): Dr. Karl Thomae GmbH, Germany
SOURCE: Ger. Offen., 18 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German

FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19510019	A1	19960926	DE 1995-19510019	19950320
WO 9629331	A1	19960926	WO 1996-EP1082	19960314
W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9651081	A1	19961008	AU 1996-51081	19960314
PRIORITY APPLN. INFO.:			DE 1995-19510019 A	19950320
			DE 1996-19600785 A	19960111
			WO 1996-EP1082 W	19960314

OTHER SOURCE(S): MARPAT 125:275902
GI



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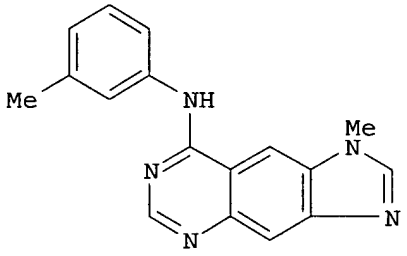

II

AB Title compds. I [Ra = H, Me; Rb = 2-naphthyl, 1,2,3,4-tetrahydro-6-naphthyl, 5-indanyl, (un)substituted Ph; Rc = H, OH, SH, Cl, NH2, CO2H, (un)substituted alkyl, etc.; Rd = (un)substituted alkyl, cycloalkyl, etc.; or RdRf or ReRf = bond; or RcRd or RcRe = alkylene with optional alkyl substitution or heteroatom replacement] and their salts, stereoisomers, and tautomers are claimed. I are inhibitors of signal transduction mediated by epidermal growth factor receptor (EGF-R), and as such are particularly useful for treating tumors and other hyperproliferative diseases. Thus, 8-(methylthio)-1H-imidazo[4,5-g]quinazoline underwent N-methylation using KOCMe3 and MeI in DMF, followed by condensation with m-toluidine at 175°, to give title compound II. The latter inhibited EGF-dependent proliferation of F/L-HERc cells in vitro with an IC50 of 0.020 μM, but inhibited IL-3-dependent proliferation with an IC50 of >1 μM.

L22 ANSWER 34 OF 34 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:371898 HCAPLUS
DOCUMENT NUMBER: 125:33669
TITLE: Preparation of 4-(phenylamino)pyrimido[5,4-d]pyrimidines as epidermal growth factor receptor antagonists
INVENTOR(S): **Himmelsbach, Frank**; Von Rueden, Thomas; Dahmann, Georg; **Metz, Thomas**
PATENT ASSIGNEE(S): Dr. Karl Thomae Gmbh, Germany
SOURCE: PCT Int. Appl., 231 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9607657	A1	19960314	WO 1995-EP3482	19950905
W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, MD, MG, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SK, TJ, TM, TT, UA, UG, UZ, VN				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
DE 4431867	A1	19960314	DE 1994-4431867	19940907
DE 19503151	A1	19960808	DE 1995-19503151	19950201
DE 19521386	A1	19961219	DE 1995-19521386	19950613
DE 19528672	A1	19970206	DE 1995-19528672	19950804
AU 9535218	A1	19960327	AU 1995-35218	19950905
AU 688972	B2	19980319		
EP 779888	A1	19970625	EP 1995-931988	19950905
EP 779888	B1	19990428		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
SK 284277	B6	20041201	SK 1997-302	19950905
NO 9701038	A	19970506	NO 1997-1038	19970306
NO 307833	B1	20000605		
BG 62969	B1	20001229	BG 1997-101289	19970306
FI 9700968	A	19970506	FI 1997-968	19970307
FI 112947	B1	20040213		
HK 1000837	A1	20001103	HK 1997-102471	19971217

PRIORITY APPLN. INFO.:	DE 1994-4431867	A	19940907
	DE 1995-19503151	A	19950201
	DE 1995-19521386	A	19950613
	DE 1995-19528672	A	19950804
	WO 1995-EP3482	W	19950905

OTHER SOURCE(S): MARPAT 125:33669
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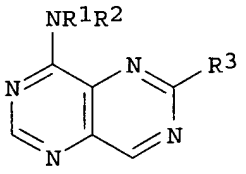

I

AB Title compds. [I; R1 = H or alkyl; R2 = (un)substituted Ph; R3 = H, halo, alkyl, alkoxy, etc.] were prepared Thus, I (R1 = H, R2 = C6H3ClF-3,4, R3 = trans 4-hydroxycyclohexylamino) had IC50 of 0.0008μM against epidermal growth factor-dependent cell growth in vitro.

=> => d stat que nos
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L5 454 SEA FILE=REGISTRY SSS FUL L3
L6 STR
L7 214 SEA FILE=REGISTRY SUB=L5 SSS FUL L6
L8 32 SEA FILE=HCAPLUS ABB=ON PLU=ON L7

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L26  ANSWER 1 OF 38  HCAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         2002:102742  HCAPLUS
DOCUMENT NUMBER:          136:275131
TITLE:                    A post-Amadori inhibitor pyridoxamine also inhibits
                          chemical modification of proteins by scavenging
                          carbonyl intermediates of carbohydrate and lipid
                          degradation
AUTHOR(S):                Voziyan, Paul A.; Metz, Thomas O.; Baynes,
                          John W.; Hudson, Billy G.
CORPORATE SOURCE:         Department of Biochemistry and Molecular Biology,
                          University of Kansas Medical Center, Kansas City, KS,
                          66160, USA
SOURCE:                   Journal of Biological Chemistry (2002), 277(5),
                          3397-3403
```

CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Reactive carbonyl compds. are formed during autoxidn. of carbohydrates and peroxidn. of lipids. These compds. are intermediates in the formation of advanced glycation end products (AGE) and advanced lipoxidn. end products (ALE) in tissue proteins during aging and in chronic disease. We studied the reaction of carbonyl compds. glyoxal (GO) and glycolaldehyde (GLA) with pyridoxamine (PM), a potent post-Amadori inhibitor of AGE formation in vitro and of development of renal and retinal pathol. in diabetic animals. PM reacted rapidly with GO and GLA in neutral, aqueous buffer, forming a Schiff base intermediate that cyclized to a hemiaminal adduct by intramol. reaction with the phenolic hydroxyl group of PM. This **bicyclic** intermediate dimerized to form a five-ring compound with a central piperazine ring, which was characterized by electrospray ionization-liquid chromatog./mass spectrometry, NMR, and x-ray crystallog. PM also inhibited the modification of lysine residues and loss of enzymic activity of RNase in the presence of GO and GLA and inhibited formation of the AGE/ALE Nε-(carboxymethyl)lysine during reaction of GO and GLA with bovine serum albumin. Our data suggest that the AGE/ALE inhibitory activity and the therapeutic effects of PM observed in diabetic animal models depend, at least in part, on its ability to trap reactive carbonyl intermediates in AGE/ALE formation, thereby inhibiting the chemical modification of tissue proteins.
REFERENCE COUNT: 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 2 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:349076 HCAPLUS
DOCUMENT NUMBER: 131:111648
TITLE: Differential increase in Fos immunoreactivity in hypothalamic and septal nuclei by arginine8-vasopressin and desglycinamide9-arginine8-vasopressin
AUTHOR(S): Lanca, A. J.; Wu, P. H.; **Jung, B.**; Liu, J.-F.; Ng, V.; Kalant, H.
CORPORATE SOURCE: Department of Pharmacology, and Psychology, University of Toronto, Toronto, ON, M5S 1A1, Can.
SOURCE: Neuroscience (Oxford) (**1999**), 91(4), 1331-1341
CODEN: NRSCDN; ISSN: 0306-4522
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The s.c. or intracerebroventricular injection of either arginine8-vasopressin or desglycinamide9-arginine8-vasopressin has been shown to facilitate memory, reduce or reverse the effects of amnesic **drugs**, and maintain tolerance to some effects of ethanol. These actions of vasopressin (and, by inference, of desglycinamide9-arginine8-vasopressin) are mediated by vasopressin V1 receptors in brain, via a c-fos-dependent mechanism, but the receptors at which the desglycinamide analog acts have not been identified. The precise central sites are also not known, but evidence of several types suggested the anterior hypothalamus and septum as probable loci of vasopressin action. In the present work, this question was studied by immunocytochem., using antibodies against Fos and Fos-like proteins. The nos. of Fos-immunoreactive nuclei were counted in several related brain regions and structures, after administration of arginine8-vasopressin, des-Gly9-[Arg8]-vasopressin or saline. A s.c. injection of vasopressin,

but not of saline, enhanced Fos expression in the paraventricular, supraoptic and suprachiasmatic nuclei of the hypothalamus, but the desglycinamide analog stimulated Fos expression only in the suprachiasmatic nucleus. Vasopressin injection significantly increased the number of Fos-immunoreactive cells in the intermediate lateral septum, medial septum, and dorsal and ventral divisions of the lateral septum. In contrast, the desglycinamide analog increased the nos. of Fos-immunoreactive cells in the dorsal and intermediate portions of the lateral septum, but caused no change in the medial septum, and a decrease in the ventral portion of the lateral septum. Increased Fos expression was also found in the subfornical organ after s.c. injection of either vasopressin or the desglycinamide analog. Double labeling with antibodies against Fos protein and against vasopressin revealed that most of the vasopressin-induced Fos-immunoreactive cells in the supraoptic, paraventricular and suprachiasmatic hypothalamic nuclei are also vasopressin immunoreactive, i.e. they are vasopressin-producing neurons. These findings suggest that a circuit involving V1 receptors in the subfornical organ, connecting fibers to the suprachiasmatic nucleus, and vasopressinergic projections from the suprachiasmatic nucleus to the lateral septum, may play a central role in mediating the actions of both vasopressin and its desglycinamide analog in the maintenance of ethanol tolerance.

REFERENCE COUNT: 76 THERE ARE 76 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 3 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:378438 HCAPLUS
DOCUMENT NUMBER: 129:135700
TITLE: The first metal-catalyzed intramolecular [5+2] cycloadditions of vinylcyclopropanes and alkenes: scope, stereochemistry, and asymmetric catalysis
AUTHOR(S): Wender, Paul A.; Husfeld, Craig O.; **Langkopf, Elke**; Love, Jennifer A.; Pleuss, Norbert
CORPORATE SOURCE: Department of Chemistry, Stanford University, Stanford, CA, 94305-5080, USA
SOURCE: Tetrahedron (**1998**), 54(25), 7203-7220
CODEN: TETRAB; ISSN: 0040-4020
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 129:135700
AB The first studies of the metal-catalyzed [5+2] cycloaddns. of vinylcyclopropanes and alkenes are described. These reactions proceed with exceptional diastereoselectivity and in good to excellent yields. The effect of tether and substituent variations are examined In addition, preliminary studies show that enantioselective cycloaddns. can be achieved through the use of catalysts modified with chiral phosphine ligands. This novel, general, and efficient procedure provides a fundamentally new approach to the synthesis of a variety of products of structural and **medicinal** significance.
REFERENCE COUNT: 79 THERE ARE 79 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 4 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:143851 HCAPLUS
DOCUMENT NUMBER: 128:204627
TITLE: First Studies of the Transition Metal-Catalyzed [5+2] Cycloadditions of Alkenes and Vinylcyclopropanes: Scope and Stereochemistry
AUTHOR(S): Wender, Paul A.; Husfeld, Craig O.; **Langkopf,**

Elke; Love, Jennifer A.
CORPORATE SOURCE: Department of Chemistry, Stanford University, Stanford, CA, 94305, USA
SOURCE: Journal of the American Chemical Society (**1998**), 120(8), 1940-1941
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 128:204627
AB The first examples of rhodium(I)-catalyzed [5+2] cycloaddns. between vinylcyclopropanes and alkenes are described along with the first studies of the scope and stereochem. of these remarkably efficient and selective processes. These cycloaddns. proceed in good to excellent yields (70-94%) and in the cases examined thus far provide only one diastereomeric cycloadduct. The product stereochem. was established through NMR studies and chemical correlations. The cycloaddn. proceeds even at high concns. (1M) and low catalyst loads (0.1 mol %) and can be conducted on the milligram to gram scale. Substitution of the internal carbon of the alkene is tolerated and leads to the efficient (>90%) formation of products possessing an angular Me group, a commonly encountered motif in numerous natural products. Similar alkyl substitution of the vinyl cyclopropane is also possible. The reaction can also be applied to the formation of 6,7-**bicyclic** systems. This procedure serves as a novel process for seven-membered ring formation and also provides the framework and substitution patterns characteristic of many biochem. and **medicinally** significant natural products and designed analogs.
REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 5 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:90330 HCAPLUS
DOCUMENT NUMBER: 128:225922
TITLE: Antagonism of the GPIIb/IIIa receptor with the nonpeptidic molecule BIBU52: inhibition of platelet aggregation in vitro and antithrombotic efficacy in vivo
AUTHOR(S): Guth, Brian D.; Seewaldt-Becker, Elke; **Himmelsbach, Frank**; Weisenberger, Hans; Muller, Thomas H.
CORPORATE SOURCE: Dep. Biological and Chemical Res., Dr. Karl Thomae GmbH, Biberach an der Riss, Germany
SOURCE: Journal of Cardiovascular Pharmacology (**1997**), 30(2), 261-272
CODEN: JCPCDT; ISSN: 0160-2446
PUBLISHER: Lippincott-Raven Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The glycoprotein (GP) IIb/IIIa (the αIIbβ3 integrin) found on platelets binds fibrinogen or von Willebrand factor when eh platelet is activated, thereby mediating the aggregation of platelets. Blockade of the GPIIb/IIIa should prevent platelet aggregation independent of the substance or substances responsible for activating the platelets. This comprehensive inhibition of platelet aggregation is though to be an effective **therapeutic** approach ti various clin. thromboembolic syndromes. This study investigated the platelet inhibition provided by blocking GPIIb/IIIa by using a new nonpeptidic mol. BIBU52, in both in vitro and in vivo models. BIBU52 competes with [125I]fibrinogen for binding sites on human platelets in a Ca2+ and pH-dependent manner with a 50% inhibitory concentration (IC50) of 35 ± 12 nM. BIBU52 inhibited the

aggregation of human platelets in platelet-rich plasma induced by collagen (1-2 μg/mL), ADP (ADP; 2.5 μM), and a thrombin receptor-activating peptide (TRAP; SFLLRNPNDKYEPFNH2; 25 μM) with IC50 values of 82, 83, and 200 nM, resp. The inhibition of platelet aggregation by BIBU52 was found to be highly species dependent. BIBU52 inhibited aggregation in plasma from rhesus and marmoset monkeys with an IC50 of 150 nM but was totally ineffective in rat plasma. The selectivity of BIBU52 for inhibiting GPIIb/IIIa in comparison with other adhesion mols. was investigated in a human endothelial cell adhesion assay. The adhesion of human cells to matrixes of vitronectin, fibronectin, collagen I, or laminin was not affected by concns. as high as 100 μM BIBU52; thus BIBU52 demonstrates a high selectivity for the human GPIIb/IIIa. The antithrombotic effect of BIBU52 in vivo was investigated in three animal models of recurrent arterial thrombus formation. In the guinea pig aorta, BIBU52 inhibited thrombus fromation dose dependently, with lack of thrombus formation for 1 h after a bolus dose of 1.0 mg/kg i.v.. Both acetylsalicylic acid and dazoxiben were less effective in this model. In pigs with recurrent thrombus formation in the carotid artery, 1.0 mg/kg i.v. also inhibited thrombus formation. Heparin was not effective in the pig, and acetylsalicylic acid was only partially effective. In the pig, the dose of 1.0 mg/kg i.v. BIBU52 also was associated with a 70% inhibition of collagen-induced platelet aggregation ex vivo but with only a transient prolongation of sublingual bleeding time to a maximum of 2.5-fold and without other hemodynamic effects. In the marmoset monkey, a dose of 10 μg/kg i.v. could abolish recurrent arterial thrombosis. Hemodynamic effects of BIBU52 in anesthetized pigs were not detected in doses ≤10 mg/kg. These data demonstrate that BIBU52 is a potent and selective antagonist of the human GPIIb/IIIa receptor and capable of substantial inhibition of platelet aggregation in vitro and ex vivo as well as inhibition of arterial thrombus formation in vivo in animal models of thrombosis.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 6 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:59116 HCAPLUS
DOCUMENT NUMBER: 128:110855
TITLE: High-throughput screening of **pharmacologically** active substances
INVENTOR(S): Czernilofsky, Armin Peter; Von Rueden, Thomas; Himmler, Adolf; Loeber, Gerhard; **Metz, Thomas** ; Schnitzer, Renate; Spevak, Walter; Stratowa, Christian; Tontsch, Ulrike; Weyer-Czernilofsky, Ulrike; Wiche-Castanon, Maria Josefa
PATENT ASSIGNEE(S): Boehringer Ingelheim International G.m.b.H., Germany; Czernilofsky, Armin Peter; Von Rueden, Thomas; Himmler, Adolf; Loeber, Gerhard; Metz, Thomas; Schnitzer, Renate; Spevak, Walter; Stratowa, Christian; et al.
SOURCE: PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9800713	A1	19980108	WO 1997-EP3329	19970625 <--

W: CA, JP, MX, US
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

EP 816848	A1	19980107	EP 1996-110459		19960628 <--
R: DE					
CA 2258022	AA	19980108	CA 1997-2258022		19970625 <--
EP 907885	A1	19990414	EP 1997-930400		19970625 <--
EP 907885	B1	20030903			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
JP 2000515964	T2	20001128	JP 1998-503822		19970625
AT 249041	E	20030915	AT 1997-930400		19970625
PT 907885	T	20040130	PT 1997-930400		19970625
ES 2203814	T3	20040416	ES 1997-930400		19970625
PRIORITY APPLN. INFO.:			EP 1996-110459	A	19960628
			WO 1997-EP3329	W	19970625

AB In a method of comparative high-throughput screening of **pharmacol** . active substances, the substances are deposited on test cells that contain ≥1 biol. target mol., the cells having an identical biol. base composition and differing in their target mols. Alternatively, the substances are deposited on cells having different biol. base compns. and identical target mols. The effect of the substance on the activity of the target mols. is measured using a detection system linked to the activation of the target mol., and is compared directly with the effect on other mols. The target mol. may be e.g. a receptor, an intracellular component of a signal-transmitting pathway (e.g. a protein kinase or adaptor mol.), a ligand-regulated transcription factor, an apoptosis-regulating proteinase, phosphatase, GTPase, or intracellular hormone receptor, in native or genetically modified form. The detection system preferably measures cell proliferation, apoptosis, or expression of reporter genes. Thus, murine FDC-P1 cells were transfected with retroviral vector pGD into which had been inserted the oncogenic form of the human cDNA for c-H-rasVal12, a marker protein and **therapeutic** target in many human tumors which is activated by posttranslational farnesylation. The IL-3-independent proliferation of the transfected cells was inhibited by the farnesyltransferase inhibitor, L 739,749. In a high-throughput assay, 1.5 + 104 cells in 100 μL growth medium were placed in each well of a microtiter plate, and test substance in DMSO was added to a final concentration of 5 μg/mL. Growth of the cells was monitored by photometry at 492 nm. Test substances which inhibited proliferation were further tested in serial dilns. in the same assay system to determine the IC50.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 7 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1997:669714 HCAPLUS

DOCUMENT NUMBER: 127:314734

TITLE: Simultaneous cocaine exposure abolishes ethanol tolerance

AUTHOR(S): Peris, J.; Sealey, S. A.; **Jung, B. J.**; Gridley, K. E.

CORPORATE SOURCE: Department of Pharmacodynamics, University of Florida, Gainesville, FL, 32610, USA

SOURCE: Behavioural Pharmacology (**1997**), 8(4), 319-330
CODEN: BPHAEL; ISSN: 0955-8810

PUBLISHER: Rapid Science Publishers

DOCUMENT TYPE: Journal

LANGUAGE: English

AB We measured changes in locomotor impairment in rats caused by ethanol exposure either given alone or simultaneously with cocaine. An initial ethanol injection (2.1 g/kg, i.p.) disrupted rotorod performance and this disruption was not significantly affected by the cocaine injection (15

mg/kg, i.p.). After 13 daily **drug** treatments, performance in the ethanol group was significantly improved whereas in the cocaine+ethanol group, performance remained disrupted to the same extent throughout testing (49±14 min). Cocaine sensitization developed after repeated exposure and this sensitization was greater in the cocaine+ethanol group. Next, all groups were tested with simultaneous ethanol and cocaine. Tolerance was not diminished in the ethanol group, whereas groups receiving saline, cocaine, or cocaine+ethanol exhibited equally disrupted behavior. During an ethanol-only test, the cocaine+ethanol groups also did not respond differently from groups receiving saline or cocaine alone. There was no difference in tolerance of the GABAA receptor to ethanol enhancement in cortical microsacs from the ethanol and cocaine+ethanol groups, nor did cocaine affect blood ethanol levels after initial or repeated exposure. A non-sensitizing dose of cocaine (7.5 mg/kg, i.p.) had no effect on the development or expression of ethanol tolerance. Cocaine disruption of ethanol tolerance thus appears to be partly due to interference of expression of ethanol tolerance by cocaine sensitization and partly due to inhibition of the development of ethanol tolerance by non-GABergic mechanisms.

REFERENCE COUNT: 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 8 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:621947 HCAPLUS
DOCUMENT NUMBER: 127:302878
TITLE: Metabolic disposition of the new fluoroquinolone antibacterial agent DW116 in rats
AUTHOR(S): Park, Y. H.; **Jung, B. H.**; Chung, B. C.; Park, J.; Mitoma, C.
CORPORATE SOURCE: Doping Control Center, Korea Institute of Science and Technology, Seoul, 130-650, S. Korea
SOURCE: Drug Metabolism and Disposition (**1997**), 25(9), 1101-1103
CODEN: DMDSAI; ISSN: 0090-9556
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The metabolic disposition of the new fluoroquinolone antibacterial agent DW116 has been studied in Sprague-Dawley rats. The compound was absorbed well and demonstrated excellent oral bioavailability. The plasma kinetic profiles were characterized by monoexponential elimination with an elimination half life of 3-4 h. The apparent mean total clearance (ClT) and the volume of distribution (V66) ranged from 221 to 274 mL/h/kg and 1.0 to 1.5 l/kg, resp., and were independent of dose between 4 and 20 mg/kg levels. The renal (ClR) clearance was 64.5 mL/h/kg and the biliary (ClB) clearance was 33.8 mL/h/kg. The combined value accounted for approx. one-half of the total clearance, indicating that the remaining one-half of the administered dose was eliminated via hepatic clearance. The major metabolite excreted in the bile was identified as the glucuronide ester of parent **drug** using base-hydrolysis of the conjugate metabolite followed by co-HPLC with standard compound, 19F-NMR and LC-MS methods. The mean urinary recoveries of free and total (free plus glucuronide ester) DW116 were 28.6% and 36.4% of the administered dose and the corresponding biliary recoveries were 14.4% and 37.0%, resp. The mass balance study after a single (100 mg/kg) oral administration of 14C-DW116 indicated complete recovery of radioactivity over a 7-day period, accounting for approx. 60-70% in feces and 30-40% in urine. 14C-DW116 extensively distributed during a prolonged process into all tissues with a rather slower penetration into the brain, lung, and muscle. The compound also

readily crossed the placenta and was transferred to the fetus.
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 9 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:618085 HCAPLUS
DOCUMENT NUMBER: 127:278211
TITLE: Novel arylglycinamide derivatives, processes for their preparation, and **pharmaceutical** compositions containing them as neurokinin antagonists
INVENTOR(S): Esser, Franz; Schnorrenberg, Gerd; Schromm, Kurt; Dollinger, Horst; **Jung, Birgit**; Speck, Georg
PATENT ASSIGNEE(S): Boehringer Ingelheim K.-G., Germany; Esser, Franz; Schnorrenberg, Gerd; Schromm, Kurt; Dollinger, Horst; Jung, Birgit; Speck, Georg
SOURCE: PCT Int. Appl., 76 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9732865	A1	19970912	WO 1997-EP1038	19970303 <--
W: AU, BG, BR, BY, CA, CN, CZ, EE, HU, IL, JP, KR, KZ, LT, LV, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
DE 19608665	A1	19970911	DE 1996-19608665	19960306 <--
CA 2247257	AA	19970912	CA 1997-2247257	19970303 <--
AU 9720943	A1	19970922	AU 1997-20943	19970303 <--
AU 718584	B2	20000413		
EP 885204	A1	19981223	EP 1997-906150	19970303 <--
EP 885204	B1	20020612		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CN 1212689	A	19990331	CN 1997-192786	19970303 <--
CN 1072664	B	20011010		
BR 9708014	A	19990727	BR 1997-8014	19970303 <--
NZ 332201	A	20000128	NZ 1997-332201	19970303
JP 2000506150	T2	20000523	JP 1997-531438	19970303
JP 3465795	B2	20031110		
AT 219069	E	20020615	AT 1997-906150	19970303
EE 3767	B1	20020617	EE 1998-302	19970303
IL 125710	A1	20020912	IL 1997-125710	19970303
PT 885204	T	20021031	PT 1997-906150	19970303
ES 2177940	T3	20021216	ES 1997-906150	19970303
SK 283052	B6	20030204	SK 1998-1207	19970303
ZA 9701850	A	19970908	ZA 1997-1850	19970304 <--
NO 9804080	A	19980904	NO 1998-4080	19980904 <--
NO 311518	B1	20011203		
HK 1019327	A1	20020208	HK 1999-102660	19990622
US 6498162	B1	20021224	US 2000-703758	20001101
US 2003092704	A1	20030515	US 2002-235053	20020905

PRIORITY APPLN. INFO.:

DE 1996-19608665	A	19960306
WO 1997-EP1038	W	19970303
US 1998-142271	B1	19981130

US 2000-703758 A1 20001101

OTHER SOURCE(S): MARPAT 127:278211

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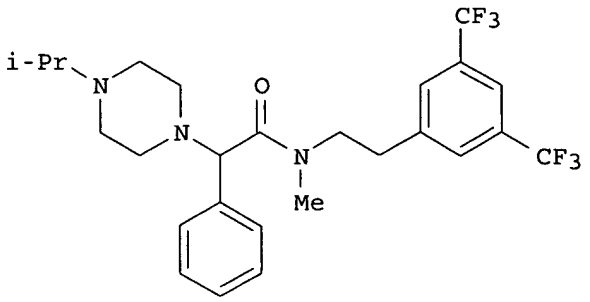

II

AB The invention relates to novel arylglycinamide derivs. R1R2NCR3(Ar)CONR4R5 I and their **pharmaceutically** acceptable salts [in which Ar = (un)substituted Ph or naphthyl, 1,3-benzodioxolyl, 1,4-benzopyranyl; NR1R2 = certain N-heterocycles; R3 = H, alkyl, (un)substituted Ph; R4 = (un)substituted phenylalkyl, naphthylalkyl; R5 = H, alkyl, cycloalkyl, CH2CO2H, CH2CONH2, OH, phenylalkyl]. Also disclosed are the production and use of I, which are valuable neurokinin (tachykinin) antagonists. For example, 1-isopropylpiperazine underwent N-alkylation by PhCHBrCO2Me (89%), followed by saponification of the ester (92%) and amidation of the resultant acid with N-methyl-3,5-bis(trifluoromethyl)phenethylamine (75%), to give title compound II, isolated as the di-HCl salt. At 1 mg/kg intraduodenally in anesthetized guinea pigs, II.2HCl gave an 80% reversal of NK1-agonist-induced hypotension.

L26 ANSWER 10 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1997:582904 HCAPLUS

DOCUMENT NUMBER: 127:243027

TITLE: Profound and sustained inhibition of platelet aggregation by Fradafiban, a nonpeptide platelet glycoprotein IIb/IIIa antagonist, and its orally active **prodrug**, Lefradafiban, in men

AUTHOR(S): Muller, Thomas H.; Weisenberger, Hans; Brickl, Rolf; Narjes, Hans; **Himmelsbach, Frank**; Krause, Jurgen

CORPORATE SOURCE: Department of Biological Research, Dr Karl Thomae GmbH, Biberach, Germany

SOURCE: Circulation (**1997**), 96(4), 1130-1138
CODEN: CIRCAZ; ISSN: 0009-7322

PUBLISHER: American Heart Association

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Clin. trials have demonstrated that platelet glycoprotein (GP) IIb/IIIa antagonists effectively prevent acute thrombotic events. Orally active GP IIb/IIIa antagonists are essential to evaluate the clin. benefit of long-term treatment. We therefore investigated platelet inhibition by the GP IIb/IIIa antagonist Fradafiban (BIBU 52; Fradafiban is the recommended INN of BIBU 52) and its orally administered **prodrug**, Lefradafiban (BIBU 104; Lefradafiban is the recommended INN of BIBU 104) in healthy subjects. The activity and plasma levels of Fradafiban and Lefradafiban were evaluated in double-blind, placebo-controlled studies in 130 healthy male subjects. One to 15 mg Fradafiban continuously infused

over 30 min reversibly inhibited platelet aggregation in platelet-rich plasma ex vivo in response to 20 μmol/L ADP (5 mg, 100% inhibition at 27 min after administration) and to both 1.0 (5 mg, 100%) and 10 μg/mL (15 mg, 97±3%) collagen. Single oral doses of Lefradafiban inhibited ADP-induced aggregation by 59±14% (50 mg [mean±SD]; n=8), 90±12% (100 mg), and 99±2% (150 mg) 8 h after administration. Correlations between activity and Fradafiban plasma levels were identical after Fradafiban and Lefradafiban treatment. After day 1, oral TID Lefradafiban treatment for 7 days inhibited aggregation by ≥31±9.6% (25 mg TID; n=8), 53±12% (50 mg; n=7), and 88±6.6% (75 mg; n=8) just before the next dose. A similar correlation between the activity and Fradafiban plasma levels was observed at days 1, 2, and 7. Oral administration of Lefradafiban maintains the potent platelet GP IIb/IIIa antagonism of Fradafiban during treatment of healthy subjects for 1 wk without signs of loss of the antiplatelet activity.

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 11 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:488457 HCAPLUS
TITLE: Transition metal-catalyzed [5+2] cycloadditions: The first studies of asymmetric induction, stereochemistry, and substituent effects.
AUTHOR(S): Wender, Paul A.; Husfeld, Craig O.; Kadereit, Dieter; **Langkopf, Elke**; Love, Jennifer A.; Pleuss, Norbert
CORPORATE SOURCE: Department Chemistry, Stanford University, Stanford, CA, 94305, USA
SOURCE: Book of Abstracts, 214th ACS National Meeting, Las Vegas, NV, September 7-11 (1997), ORGN-053. American Chemical Society: Washington, D. C.
CODEN: 64RNAO
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English
AB The generation of medium-sized rings bearing complex functionality is a considerable challenge and has inspired much effort to develop methodol. to resolve this synthetic problem. Cycloaddns., which allow for facile formation of complex ring systems, have recently become an attractive approach to medium-sized ring synthesis. Due to the prevalence of seven-membered rings in natural products, many convenient syntheses of seven-membered rings via cycloaddns. have emerged in recent years. In conjunction with our continuing study of transition metal-catalyzed cycloaddns., we recently reported the first example of a transition metal-catalyzed intramol. [5+2] cycloaddn. between tethered vinylcyclopropane and alkyne units, generating a [5.3.0] **bicyclic** ring system. We herein report the first examples of rhodium(I)-catalyzed [5+2] cycloaddns. between vinylcyclopropanes and alkenes and preliminary results involving the use of asym. ligands in the cycloaddn. Addnl., we wish to report the cycloaddns. of substrates bearing substitution on the cyclopropane ring. [Equation Omitted].

L26 ANSWER 12 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:400093 HCAPLUS
DOCUMENT NUMBER: 127:17681
TITLE: Five-membered heterocycles [thiazoles, imidazoles, and thiadiazoles], **pharmaceutical** agents containing them, their use as aggregation inhibitors, and methods for their production
INVENTOR(S): Linz, Guenter; **Himmelsbach, Frank**; Pieper, Helmut; Austel, Volkhard; Guth, Brian; Weisenberger,

Johannes
PATENT ASSIGNEE(S): Dr. Karl Thomae Gmbh, Germany
SOURCE: PCT Int. Appl., 120 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9715567	A1	19970501	WO 1996-EP4390	19961010 <--
W: CA, JP, MX				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
DE 19539091	A1	19970424	DE 1995-19539091	19951020 <--
DE 19548798	A1	19970703	DE 1995-19548798	19951227 <--
EP 858457	A1	19980819	EP 1996-934603	19961010 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 11513382	T2	19991116	JP 1996-513786	19961010

PRIORITY APPLN. INFO.: DE 1995-19539091 A 19951020
DE 1995-19548798 A 19951227
WO 1996-EP4390 W 19961010
OTHER SOURCE(S): MARPAT 127:17681
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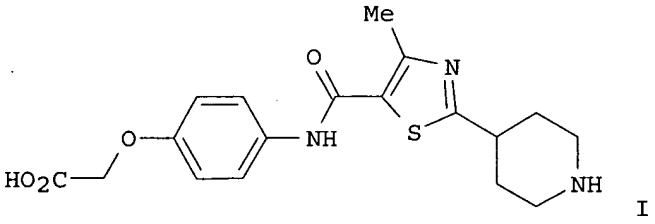


I

AB Disclosed are certain five-membered heterocycles, their tautomers, stereoisomers, mixts., and salts, having valuable **pharmacol.** properties, especially cellular aggregation-inhibiting properties. Also disclosed are **pharmaceutical** agents containing the compds., their use, and methods of producing them. The compds. have antiinflammatory, osteoporosis-inhibiting, antithrombotic, antiaggregatory, and tumor- and metastasis-inhibiting properties. Prepns. of approx. 100 invention compds. and 60 intermediates are described, and six standard **pharmaceutical** formulations are given. The example compound I.HBr had an EC50 of 0.13 μM for inhibition of collagen-induced platelet aggregation in vitro.

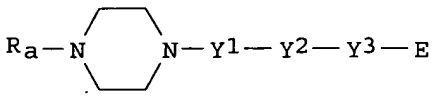
L26 ANSWER 13 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:137705 HCAPLUS
DOCUMENT NUMBER: 126:180885
TITLE: Empirical **monotherapy** with meropenem versus imipenem/cilastatin for febrile episodes in neutropenic patients
AUTHOR(S): Shah, P. M.; Heller, A.; Fuhr, H.-G.; Walther, F.; Halir, S.; Schaumann, R.; Boehme, A.; **Jung, B.** ; Koehler, A.; Lips-Schulte, C.; Stille, W.
CORPORATE SOURCE: Medizinische Klinik III, Schwerpunkt Infektiologie,

Frankfurt, D-60590, Germany
SOURCE: Infection (Munich) (**1996**), 24(6), 480-484
CODEN: IFTNAL; ISSN: 0300-8126
PUBLISHER: MMV Medizin Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In a nonblind, randomized, parallel-group study, initial empirical **monotherapy** with meropenem 1 g i.v. every 8 h was compared to an identical dosage of imipenem/cilastatin for the treatment of 66 febrile episodes in 61 adult neutropenic patients. 25/31 Episodes treated with meropenem and 24/30 imipenem/cilastatin-treated episodes were still receiving unmodified **therapy** at 72 h (primary endpoint); this difference was not statistically significant. By the end of the treatment courses, 18/31 meropenem-treated episodes had responded clin. (cured or improved) compared with 18/30 episodes treated with imipenem/cilastatin. Another ten episodes initially treated with meropenem and six episodes treated with imipenem/cilastatin were cured after an addnl. antimicrobial agent had been administered (cured with modification). Satisfactory bacteriol. responses (eradication plus presumed eradication) at the end of unmodified **therapy** was 9/11 in the meropenem group and 14/16 in the comparator group. Both regimes were well tolerated; however, there were more reports of nausea and/or vomiting in the imipenem/cilastatin group (7/33 vs. 2/33 in the meropenem group). The carbapenems meropenem and imipenem/cilastatin appear to be suitable agents for empirical **monotherapy** of febrile episodes in neutropenic patients. Meropenem may be better tolerated than imipenem/cilastatin, allowing optimal dosing in this patient population.

L26 ANSWER 14 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:483488 HCAPLUS
DOCUMENT NUMBER: 125:142582
TITLE: Piperazine derivatives: **medicaments** containing them, their use, and processes for their preparation
INVENTOR(S): Pieper, Helmut; Austel, Volkhard; **Himmelsbach, Frank**; Linz, Guenther; Guth, Brian; Weisenberger, Johannes
PATENT ASSIGNEE(S): Thomae, Dr. Karl, G.m.b.H., Germany
SOURCE: Eur. Pat. Appl., 45 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
EP 718287	A2	19960626	EP 1995-120118		19951219 <--
EP 718287	A3	19970129			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE					
DE 4446300	A1	19960627	DE 1994-4446300		19941223 <--
DE 19533224	A1	19970313	DE 1995-19533224		19950908 <--
US 5700801	A	19971223	US 1995-572256		19951213 <--
AU 9540558	A1	19960704	AU 1995-40558		19951219 <--
CA 2165922	AA	19960624	CA 1995-2165922		19951221 <--
BR 9505981	A	19971223	BR 1995-5981		19951221 <--
CN 1131665	A	19960925	CN 1995-121745		19951223 <--
JP 08231509	A2	19960910	JP 1995-336774		19951225 <--
PRIORITY APPLN. INFO.:			DE 1994-4446300	A	19941223
			DE 1995-19533224	A	19950908

OTHER SOURCE(S): CASREACT 125:142582; MARPAT 125:142582
GI



I

AB The preparation of title compds. I [Ra = substituted pyridyl group; Y1 = CO, COCO, substituted CO, (un)substituted SO2, aminocarbonyl, etc.; Y2 = (un)substituted 1,3- or 1,4-phenylene, 3- or 4-piperidinyl, etc.; Y3 = CH2CO, CH2CH2CO, OCH2CO, etc.; E = OH, OMe, OEt, Me3CO, etc.], useful as antithrombotics and blood platelet aggregation inhibitor, is described. Thus, condensation of 1-(4-pyridyl)piperazine with Me acrylate in the presence of methanolic solution of benzyltrimethylammonium hydroxide in CHCl3 followed by LiOH hydrolysis gave 3-[4-(4-pyridyl)piperazin-1-yl]propionic acid which on treatment with Me p-trans-aminocyclohexanecarboxylate hydrochloride in the presence of 2-(1H-benzotriazol-1-yl)-1,1,3,3-tetramethyluronium tetrafluoroborate-1-hydroxy-1H-benzotriazole-N-methylmorpholine in DMF gave title compound, Me [4-trans-[3-[4-(4-pyridyl)piperazin-1-yl]propionyl]amino]cyclohexanecarboxylate. Antithrombotic and blood platelet aggregation inhibitor activity of some of the compds. prepared is given.

L26 ANSWER 15 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:323139 HCAPLUS
DOCUMENT NUMBER: 125:10849
TITLE: Preparation of arylpiperazinylethylamines and related compounds as neurokinin antagonists.
INVENTOR(S): Dollinger, Horst; Schnorrenberg, Gerd; Briem, Hans; **Jung, Birgit**; Speck, Georg
PATENT ASSIGNEE(S): Boehringer Ingelheim Kg, Germany
SOURCE: Ger. Offen., 38 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19520499	A1	19960321	DE 1995-19520499	19950603 <--
DE 19520499	C2	20030618		
US 5696123	A	19971209	US 1995-473423	19950607 <--
US 5708006	A	19980113	US 1995-476987	19950607 <--
CA 2200083	AA	19960321	CA 1995-2200083	19950913 <--
WO 9608480	A1	19960321	WO 1995-EP3605	19950913 <--
W: AU, BR, CA, CN, CZ, FI, HU, JP, KR, LT, LV, MX, NO, NZ, PL, RU, SI, SK, UA, US, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9535671	A1	19960329	AU 1995-35671	19950913 <--
EP 781277	A1	19970702	EP 1995-932739	19950913 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 10505826	T2	19980609	JP 1995-509913	19950913 <--
US 5985881	A	19991116	US 1997-905251	19970802
US 6235732	B1	20010522	US 1999-250342	19990216
US 6191135	B1	20010220	US 2000-499913	20000208

PRIORITY APPLN. INFO.:

DE 1994-4433208	A1	19940917
DE 1995-19520499	A	19950603
US 1995-473423	A3	19950607
WO 1995-EP3605	W	19950913
US 1997-905251	A3	19970802
US 1999-250342	A1	19990216

OTHER SOURCE(S): MARPAT 125:10849

AB ACR1ZCH2R2BX(R3)m [A = Ar, ArCH2, ArCHPh, Ar(CH2)2, etc.; Ar = (substituted) Ph, naphthyl, pyridyl, thienyl; B = CHR12, CH2CH2, CO, CONH, COCH2, COCH2CH2; R12 = H, Me; R1 = H, alkyl, Ph; R2 = H, (Ph-substituted) alkyl, alkylcarbonyl; R3 = H, alkyl, fluoroalkyl, halo, alkoxy; m = 1-3; Z = dialkylamino, (substituted) piperazinyl, piperidinyl, pyrrolidinyl, morpholinyl, thiomorpholinyl, etc.; X = Ph ring], were prepared Thus, a mixture of N-phenylpiperazine and 2-methoxybenzaldehyde in Et2O/1N HCl at 0° was treated with aqueous KCN and stirred overnight to give 76% 2-(2-methoxyphenyl)-2-(4-phenylpiperazin-1-yl)acetonitrile. This was treated with LiAlH4/H2SO4 in Et2O/THF to give 92% 2-(2-methoxyphenyl)-2-(4-phenylpiperazin-1-yl)ethylamine. The latter was treated with 3,5-bis(trifluoromethyl)benzaldehyde and NaBH3CN in MeOH to give 73% N-3,5-bis(trifluoromethyl)benzyl-[2-(2-methoxyphenyl)-2-(4-phenylpiperazin-1-yl)]ethylamine. Title compds. inhibited binding of 125I-marked substance P to NK1 receptors with Ki = 2-909 nM.

L26 ANSWER 16 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1996:303724 HCAPLUS

DOCUMENT NUMBER: 124:343122

TITLE: Preparation of arylpiperidines as cell-cell and cell-matrix interaction inhibitors.

INVENTOR(S): Pieper, helmut; Austel, Volkhard; **Himmelsbach, Frank**; Linz, Guenter; Guth, Brian; Weisenberger, Johannes

PATENT ASSIGNEE(S): Dr. Karl Thomae Gmbh, Germany

SOURCE: Ger. Offen., 14 pp.
CODEN: GWXXBX

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
DE 4431868	A1	19960314	DE 1994-4431868	19940907	<--

PRIORITY APPLN. INFO.: DE 1994-4431868 19940907

OTHER SOURCE(S): MARPAT 124:343122

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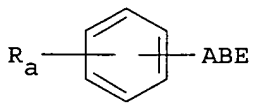


I

AB Title compds. [I; Ra = piperidinyl, piperazinyl, piperazino; A = CH:CHCO, CH2CH2CO, NR1CH2CO; R1 = H, alkyl; B = NR1-cyclohexylene, piperidinylene, NR1(CH2)n; n = 2, 3; E = CO2H, alkoxycarbonyl, cycloalkoxycarbonyl], were prepared Thus, 4-[4-[[trans-4-(4-carboxycyclohexyl)]aminocarbonyl(trans-ethylene)]phenyl]piperidine hydrochloride [preparation from 1-acetyl-4-phenylpiperidine via 4-(4-piperidinyl)-trans-cinnamic acid

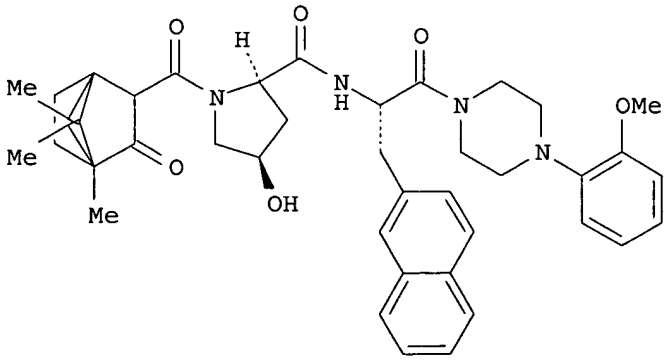
given] inhibited blood platelet aggregation with EC50 = 350 nM.

L26 ANSWER 17 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:155518 HCAPLUS
DOCUMENT NUMBER: 124:203106
TITLE: Preparation of modified peptides as neurokinin (tachykinin) antagonists
INVENTOR(S): Schnorrenberg, Gerd; Esser, Franz; Dollinger, Horst; **Jung, Birgit**; Speck, Georg; Buerger, Erich
PATENT ASSIGNEE(S): Boehringer Ingelheim KG, Germany; Boehringer Ingelheim International GmbH
SOURCE: PCT Int. Appl., 100 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9530687	A1	19951116	WO 1995-EP1691	19950504 <--
W: AU, BG, BY, CA, CN, CZ, EE, FI, HU, JP, KR, KZ, LT, LV, MX, NO, NZ, PL, RO, RU, SG, SI, SK, UA, UZ, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
DE 4445939	A1	19951109	DE 1994-4445939	19941222 <--
AU 9525249	A1	19951129	AU 1995-25249	19950504 <--
AU 690275	B2	19980423		
EP 804463	A1	19971105	EP 1995-919392	19950504 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV				
JP 09512806	T2	19971222	JP 1995-528677	19950504 <--
RO 115355	B1	20000128	RO 1996-2085	19950504
NO 9604700	A	19961106	NO 1996-4700	19961106 <--
FI 9604473	A	19961107	FI 1996-4473	19961107 <--

PRIORITY APPLN. INFO.: DE 1994-4416255 A 19940507
DE 1994-4445939 A 19941222
WO 1995-EP1691 W 19950504

OTHER SOURCE(S): MARPAT 124:203106
GI



I

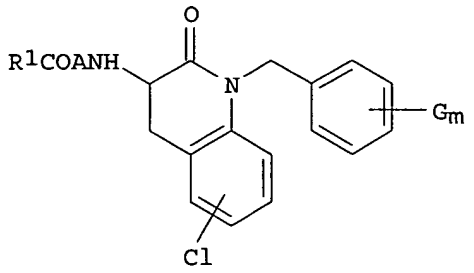
AB The production and use of new amino acid derivs. of general formula

R1-R11-A1-B [R1 = saturated or partially saturated 6-membered ring optionally containing and O or N atom and/or a CH2, CMe2, CEt2, or CH2CH2 bridge, and containing and O, OH, or alkoxy group in the 2- or 3 position; R11 = CO, CH2CO, SO2, CH2SO2; A1 = optionally modified or protected amino acid residue; B = A2NR2R3, R5; A2 = lipophilic amino acid residue; R2, R3 = alkyl, aralkyl, heteroaryl, etc., NR2R3 = heterocyclic ring; R5 = amino-substituted lactam ring system] and **pharmaceutically** acceptable salts thereof, were prepared as valuable neurokinin (tachykinin) antagonists. Thus, camphor-substituted dipeptide amide I, prepared by stepwise couplings, showed neurokinin 1 (NK1) receptor affinity IC50 = 3.1 nM and NK2 affinity IC50 = 21 nM.

L26 ANSWER 18 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:990646 HCAPLUS
DOCUMENT NUMBER: 124:30435
TITLE: Preparation of peptide analogs as tachykinin antagonists.
INVENTOR(S): Esser, Frank; Schnorrenberg, Gerd; Dollinger, Horst; **Jung, Birgit**; Buerger, Erich; Speck, Georg
PATENT ASSIGNEE(S): Boehringer Ingelheim KG, Germany
SOURCE: Ger. Offen., 9 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
DE 4406885	A1	19950907	DE 1994-4406885	19940303	<--
CA 2182396	AA	19950908	CA 1995-2182396	19950302	<--
WO 9523810	A1	19950908	WO 1995-EP760	19950302	<--
W: AU, CA, CN, CZ, FI, HU, JP, KR, MX, NO, NZ, PL, RU, SI, UA, VN					
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
AU 9518127	A1	19950918	AU 1995-18127	19950302	<--
CN 1142228	A	19970205	CN 1995-191895	19950302	<--
JP 09505317	T2	19970527	JP 1995-522700	19950302	<--
JP 2801087	B2	19980921			
HU 75527	A2	19970528	HU 1996-2402	19950302	<--
EP 802922	A1	19971029	EP 1995-909796	19950302	<--
EP 802922	B1	20010926			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE					
AT 206135	E	20011015	AT 1995-909796	19950302	
NO 9603655	A	19961101	NO 1996-3655	19960902	<--
FI 9603440	A	19960903	FI 1996-3440	19960903	<--
US 5922878	A	19990713	US 1997-863757	19970527	<--
PRIORITY APPLN. INFO.:			DE 1994-4406884 A	19940303	
			DE 1994-4406885 A	19940303	
			WO 1995-EP760 W	19950302	
			US 1995-398257 B1	19950303	

OTHER SOURCE(S): MARPAT 124:30435
GI



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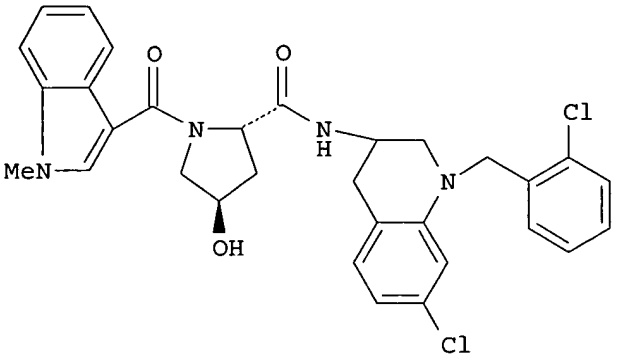

II

AB Title compds. [I; R1 = vinyl, aryl, heteroaryl, heteroaralkyl, arylvinyl, aryloxyalkyl, arylalkoxy, cycloalkyl, cycloalkylalkyl, (methyl-substituted) **bicycloheptyl**, **bicycloheptylalkyl**, adamantyl, adamantylalkyl, decalinyl, decalinylalkyl, tetralinyl, tetralinylalkyl, diphenylalkyl, aralkylaminoalkyl, etc.; A = D- or L-Ala, -Val, -Leu, -Phe, -Trp, -hydroxyprolyl, -His, -azetidin-2-carbonyl, -Orn, -pyroglutaminyl, etc.; G = F, Cl, Br, Me, Et, MeO; m = 1-5], were prepared Thus, 3-amino-1-(2-chlorobenzyl)-7-chloro-1,2,3,4-tetrahydroquinolin-2-one hydrochloride (preparation given) was coupled to (2s,4r)-N-(1-methylindol-3-ylcarbonyl)-4-hydroxyproline in DMF containing Et3 and TBTU to give title compound (II) as a mixture of diastereomers.

L26 ANSWER 19 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:990645 HCAPLUS
DOCUMENT NUMBER: 124:30434
TITLE: Preparation of peptide derivatives as neurokinin antagonists.
INVENTOR(S): Esser, Frank; Schnorrenberg, Gerd; Dollinger, Horst; **Jung, Birgit**; Buerger, Erich
PATENT ASSIGNEE(S): Boehringer Ingelheim KG, Germany
SOURCE: Ger. Offen., 13 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4406884	A1	19950907	DE 1994-4406884	19940303 <--
CA 2182396	AA	19950908	CA 1995-2182396	19950302 <--
WO 9523810	A1	19950908	WO 1995-EP760	19950302 <--

W: AU, CA, CN, CZ, FI, HU, JP, KR, MX, NO, NZ, PL, RU, SI, UA, VN					
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
AU 9518127	A1	19950918	AU 1995-18127	19950302	<--
ZA 9501728	A	19951221	ZA 1995-1728	19950302	<--
CN 1142228	A	19970205	CN 1995-191895	19950302	<--
JP 09505317	T2	19970527	JP 1995-522700	19950302	<--
JP 2801087	B2	19980921			
HU 75527	A2	19970528	HU 1996-2402	19950302	<--
EP 802922	A1	19971029	EP 1995-909796	19950302	<--
EP 802922	B1	20010926			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE					
AT 206135	E	20011015	AT 1995-909796	19950302	
US 5712397	A	19980127	US 1995-467428	19950606	<--
NO 9603655	A	19961101	NO 1996-3655	19960902	<--
FI 9603440	A	19960903	FI 1996-3440	19960903	<--
US 5922878	A	19990713	US 1997-863757	19970527	<--
PRIORITY APPLN. INFO.:			DE 1994-4406884	A 19940303	
			DE 1994-4406885	A 19940303	
			WO 1995-EP760	W 19950302	
			US 1995-398257	A1 19950303	

OTHER SOURCE(S): MARPAT 124:30434

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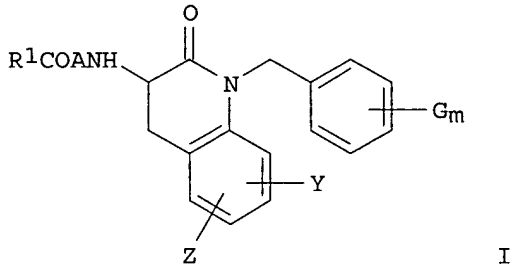

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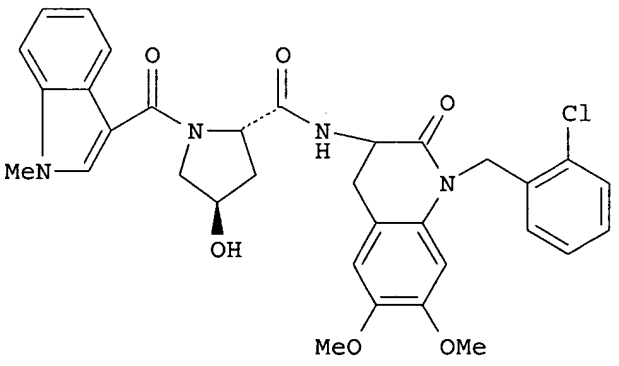


II

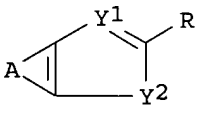
AB Title compds. [I; R1 = vinyl, aryl, heteroaryl, arylvinyl, heteroarylvinyl, aryoxyalkyl, aralkoxy, (methyl-substituted) **bicycloheptyl**, adamantyl, adamantylalkyl, decalinyl, tetralinyl, diphenylalkyl, aralkylaminoalkyl, etc.; A = D- or L-Ala, -Val, -Leu, -Ile, -Ser, -Thr, -Cys, -Met, -Phe, -Tyr, -Pro, -Trp, -didehydroprolyl, -pyroglutamyl, -His, -4-hydroxyprolyl, 4-mercaptoprolyl, -Orn, etc.; G = F, Cl, Br, Et; m = 1-5; Y, Z = H, alkyl, alkoxy, (substituted) PhCH2O, CF3, OCF3, halo, etc.; vicinal YZ = OCH2O, OCH2CH2O, (CH2)4], were prepared

as tachykinin antagonists (no data). Thus, 3-amino-1-(2-chlorobenzyl)-6,7-dimethoxy-1,2,3,4-tetrahydroquinolin-2-one hydrochloride (preparation from 6-nitroveratryl alc. given) was coupled with (2s,4R)-N-(1-methylindol-3-ylcarbonyl)-4-hydroxyproline in DMF using TBTU to give title compound (II) as a separable mixture of diastereomers.

L26 ANSWER 20 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:789124 HCAPLUS
DOCUMENT NUMBER: 123:198796
TITLE: Preparation of **bicyclic** heterocycles as cell-cell and cell-matrix interaction inhibitors
INVENTOR(S): Linz, Guenter; **Himmelsbach, Frank**; Pieper, Helmut; Austel, Volkhard; Mueller, Thomas; Weisenberger, Johannes; Guth, Brian
PATENT ASSIGNEE(S): Dr. Karl Thomae G.m.b.H., Germany
SOURCE: Ger. Offen., 26 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4324580	A1	19950126	DE 1993-4324580	19930722
EP 639575	A1	19950222	EP 1994-111221	19940719
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
CA 2128464	AA	19950123	CA 1994-2128464	19940720
JP 07070137	A2	19950314	JP 1994-168505	19940721
US 5607944	A	19970304	US 1995-509248	19950731
PRIORITY APPLN. INFO.:			DE 1993-4324580 A	19930722
			US 1994-278435 B1	19940721

OTHER SOURCE(S): CASREACT 123:198796; MARPAT 123:198796
GI



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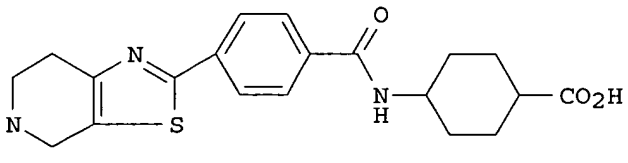


II

AB Title compds. [I; A = N:CHNR2(CH2)m, CH:CHN:CH, (CH2)nNR2(CH2)p, etc.; R = Z1Z2Z3Z4R10; R2 = H, (phenyl)alkyl, alkoxycarbonyl, etc.; R10 = CO2H, alkoxycarbonyl, etc.; Y1 = N, CR1; R1 = H, alkyl; Y2 = NR1, O, S; Z1 = C6H4, 1,4-cyclohexylene, 1,4-piperidylene, etc.; Z2 = CO, CH2, CH2SO2, etc.; Z3 = 1,4-cyclohexylene, 1,4-piperidylene, etc.; Z4 = bond, alkylene, etc.] were prepared Thus, 4-(NC)C6H4CO2Et was thiolized and the product cyclocondensed with 3-bromopiperidin-4-one hydrobromide to give, in 2 addnl. steps, 5-tert-butoxycarbonyl-2-(4-carboxyphenyl)-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine which was amidated by Me trans-4-aminocyclohexanecarboxylate to give, after deprotection and saponification, title compound II. The latter had IC50 of 100nM against collagen-induced platelet aggregation in vitro.

L26 ANSWER 21 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:550906 HCAPLUS
DOCUMENT NUMBER: 122:314547
TITLE: Preparation of urea residue-substituted heterocyclic compounds with antithrombotic, antineoplastic and blood platelet-aggregation inhibition activities
INVENTOR(S): **Himmelsbach, Frank**; Pieper, Helmut; Austel, Volkhard; Linz, Guenter; Guth, Brian; Mueller, Thomas; Weisenberger, Johannes
PATENT ASSIGNEE(S): Dr. Karl Thomae GmbH, Germany
SOURCE: Eur. Pat. Appl., 81 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 612741	A1	19940831	EP 1994-102557	19940221 <--
EP 612741	B1	19980610		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
DE 4305388	A1	19940825	DE 1993-4305388	19930222 <--
DE 4332168	A1	19950323	DE 1993-4332168	19930922 <--
EE 3397	B1	20010416	EE 1994-311	19941123
PRIORITY APPLN. INFO.:			DE 1993-4305388 A	19930222
			DE 1993-4332168 A	19930922

OTHER SOURCE(S): MARPAT 122:314547
AB The title compds., which contain urea-like moieties, often in the form of divalent imidazolidinone groups, which demonstrate a combination of antithrombotic, antineoplastic (no data), and blood platelet-aggregation inhibition activities, are prepared and **pharmaceutical** dosage forms containing them presented. Thus, 1-[4-(2-carboxyethyl)phenyl]-3-(1,2,3,4-tetrahydroisoquinolin-6-yl)imidazolidin-2-one was prepared and demonstrated ED50 for blood platelet aggregation inhibition of 40 nM.

L26 ANSWER 22 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:437898 HCAPLUS
DOCUMENT NUMBER: 122:207131
TITLE: Abuse of marijuana and its verification
AUTHOR(S): **Jung, B. C.**
CORPORATE SOURCE: Korea Inst. Sci. Technol., S. Korea
SOURCE: Hwahak Sekye (**1994**), 34(4), 323-4
CODEN: HWSEEX; ISSN: 1225-004X
PUBLISHER: Korean Chemical Society
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Korean
AB A review, with no refs., of the chemical, **pharmacol.**, and abuse of marijuana. Different methods of detecting marijuana metabolites in human are discussed.

L26 ANSWER 23 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:304885 HCAPLUS
DOCUMENT NUMBER: 122:106532
TITLE: Preparation of amino acid- and peptideamides as tachykinin antagonists
INVENTOR(S): Esser, Franz; Schnorrenberg, Gerd; Dollinger, Horst; **Jung, Birgit**; Buerger, Erich
PATENT ASSIGNEE(S): Boehringer Ingelheim KG, Germany; Boehringer Ingelheim International GmbH

SOURCE: PCT Int. Appl., 152 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9405693	A1	19940317	WO 1993-EP2329		19930828
W: AU, BG, BY, CA, CZ, FI, HU, JP, KR, NO, NZ, PL, RU, SK, UA					
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
DE 4243496	A1	19940310	DE 1992-4243496		19921222
DE 4315437	A1	19941110	DE 1993-4315437		19930508
EP 610487	A1	19940817	EP 1993-919208		19930828
EP 610487	B1	19991110			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE					
JP 07501085	T2	19950202	JP 1993-506852		19930828
AU 677792	B2	19970508	AU 1993-49547		19930828
AU 9349547	A1	19940329			
CN 1086222	A	19940504	CN 1993-117349		19930903
FI 9401987	A	19940429	FI 1994-1987		19940429
NO 9401611	A	19940502	NO 1994-1611		19940502
GR 3032395	T3	20000531	GR 2000-400089		20000114
PRIORITY APPLN. INFO.:			DE 1992-4229447	A	19920903
			DE 1992-4243496	A	19921222
			DE 1993-4315437	A	19930508
			WO 1993-EP2329	W	19930828

OTHER SOURCE(S): MARPAT 122:106532
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB R1COA1B [I; R1 = vinyl, (substituted) aryl, heteroaryl, aralkyl, heteroarylalkyl, cycloalkyl, adamantyl, adamantylalkyl, decalinyl, decalinalkyl, (methyl)**bicycloheptyl**, etc.; A1 = D- or L-Ala, D- or L-Val, D- or L-Leu, D- or L-Ile, D- or L-Thr, D- or L-Cys, D- or L-Phe, D- or L-Trp, D- or L-Pro, D- or L-dehydroPro, D- or L-pGlu, D- or L-Asp, D- or L-Asn, D- or L-Lys, D- or L-Orn, etc.; B = A2NR2R3, R5; A2 = lipophilic α-amino acid residue; R2, R3 = alkyl, OH, (substituted) aralkyl, heteroaryl; NR2R3 = Q1, Q2; m, n = 0-3; m+n = 2-5; s = 2,3; R5 = Q3, Q4; W = Q5, Q6, diarylmethyl, cyclopentyl, etc.; R6 = (substituted) aralkyl, diarylalkyl, heteroarylalkyl, phenylaminoalkyl, naphthylaminoalkyl, etc.; R7 = H, alkyl; X = H2, O; Y, Z = H, alkyl, alkoxy, (substituted) PhCH2O; t, u = 0, or t = 1, u = 0, or t, u = 1, or t = 2, u = 0], were prepared Thus, title compound II, prepared by solution phase couplings, bound to substance P receptors with IC50 = 60 nM.

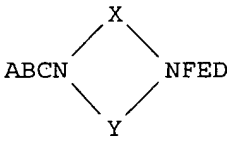
L26 ANSWER 24 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:289966 HCAPLUS
DOCUMENT NUMBER: 122:81372
TITLE: Preparation of cyclic urea derivatives as **drugs**
INVENTOR(S): **Himmelsbach, Frank**; Austel, Volkhard; Linz, Guenter; Pieper, Helmut; Guth, Brian; Mueller, Thomas; Weisenberger, Johannes
PATENT ASSIGNEE(S): Thomae, Dr. Karl, G.m.b.H., Germany

SOURCE: Eur. Pat. Appl., 125 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
EP 587134	A2	19940316	EP 1993-114401	19930908	<--
EP 587134	A3	19940706			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE					
DE 4230470	A1	19940414	DE 1992-4230470	19920911	<--
DE 4302052	A1	19940728	DE 1993-4302052	19930126	<--
DE 4309213	A1	19940929	DE 1993-4309213	19930322	<--
FI 9303942	A	19940312	FI 1993-3942	19930909	<--
CA 2105934	AA	19940312	CA 1993-2105934	19930910	<--
NO 9303248	A	19940314	NO 1993-3248	19930910	<--
AU 9346249	A1	19940324	AU 1993-46249	19930910	<--
ZA 9306689	A	19950310	ZA 1993-6689	19930910	<--
HU 71496	A2	19951128	HU 1993-2577	19930910	<--
US 5681841	A	19971028	US 1993-120008	19930910	<--
CN 1092769	A	19940928	CN 1993-114711	19930911	<--
JP 06263740	A2	19940920	JP 1993-226864	19930913	<--
US 5880284	A	19990309	US 1997-864528	19970528	<--

PRIORITY APPLN. INFO.:	DE 1992-4230470	A	19920911
	DE 1993-4302052	A	19930126
	DE 1993-4309213	A	19930322
	US 1993-120008	A3	19930910

OTHER SOURCE(S): MARPAT 122:81372
GI



I

AB Title compds. [I; A = e.g., acylamidino, etc.; B = e.g., 1,4-azacycloheptylene, 1,4- piperidinylene, 1,4-piperazinylene, etc.; C = e.g., 1,4- piperidinylene, 1,2,3,4-tetrahydro-2,6-naphthylene, 1,4-**bicyclo**[2.2.2]octanylene, etc.; D = alkylene, 1,3-phenylene, 1,4-cyclohexylene, etc.; E = bond, CH:CH, alkylene, etc.; F = CO2H, alkoxycarbonyl, etc.; X = e.g., N-cyanocarbimino, etc.; Y = e.g., 1,2-cyclohexylene] were prepared as cell aggregation inhibitors. Thus, 2-(4-amidinophenyl)-4-[4-[2-(cyclohexyloxycarbonyl)ethyl]phenyl]-5-methyl-4H-1,2,4-triazol-3-one hydrochloride inhibited ex vivo thrombocyte aggregation in blood from rhesus monkeys after oral administration of 1mg/kg.

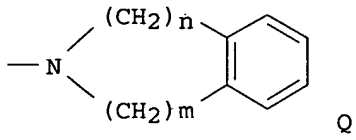
L26 ANSWER 25 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1994:701326 HCAPLUS
DOCUMENT NUMBER: 121:301326
TITLE: Preparation of new dipeptide derivatives as neurokinin antagonists
INVENTOR(S): Schnorrenberg, Gerd; Esser, Franz; Dollinger, Horst; **Jung, Birgit**; Buerger, Erich

PATENT ASSIGNEE(S): Boehringer Ingelheim KG, Germany
SOURCE: Ger. Offen., 49 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

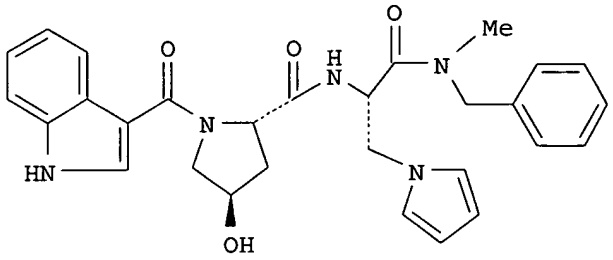
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
DE 4243496	A1	19940310	DE 1992-4243496	19921222	<--
WO 9405693	A1	19940317	WO 1993-EP2329	19930828	<--
W: AU, BG, BY, CA, CZ, FI, HU, JP, KR, NO, NZ, PL, RU, SK, UA					
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
EP 610487	A1	19940817	EP 1993-919208	19930828	<--
EP 610487	B1	19991110			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE					
JP 07501085	T2	19950202	JP 1993-506852	19930828	<--
HU 70475	A2	19951030	HU 1994-1323	19930828	<--
AU 677792	B2	19970508	AU 1993-49547	19930828	<--
AU 9349547	A1	19940329			
AT 186548	E	19991115	AT 1993-919208	19930828	
ES 2137998	T3	20000101	ES 1993-919208	19930828	
EP 979827	A1	20000216	EP 1999-100929	19930828	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE					
ZA 9306472	A	19940627	ZA 1993-6472	19930902	<--
US 5596000	A	19970121	US 1993-116090	19930902	<--
FI 9401987	A	19940429	FI 1994-1987	19940429	<--
NO 9401611	A	19940502	NO 1994-1611	19940502	<--
US 5849918	A	19981215	US 1995-460964	19950605	<--
US 6147212	A	20001114	US 1998-111498	19980708	
GR 3032395	T3	20000531	GR 2000-400089	20000114	

PRIORITY APPLN. INFO.:	DE 1992-4229447	A1	19920903
	DE 1992-4243496	A	19921222
	DE 1993-4315437	A	19930508
	EP 1993-919208	A3	19930828
	WO 1993-EP2329	W	19930828
	US 1993-116090	A3	19930902
	US 1995-460964	A3	19950605

OTHER SOURCE(S): CASREACT 121:301326; MARPAT 121:301326
GI



Q



II

AB Title compds. R1-CO-A1-A2-NR2R3 [I; R1 = vinyl, aryl, heteroaryl, aralkyl, heteroaralkyl, arylvinyl, heteroarylvinyl, etc.; A1 = D- or L-Ala, -Val, -Leu, etc.; A2 = α-amino acid residue, etc; R2, R3 = alkyl; or NR2R3 = heterocycle residue such as Q; m, n = 0, 1, 2, 3], useful as neurokinin antagonists (no data), are prepared E.g., L-Z-3-(1-pyrrolyl)alanine Me ester was stirred with 2,5-dimethoxytetrahydrofurn in H2O-EtOAc at room temperature for 23 h to give, after treatment with aqueous NaHCO3, Z-Pal-OMe [Pal = 3-(1-pyrrolyl)alanine residue], which was hydrolyzed to give Z-Pal-OH, which was amidated with N-methylbenzylamine to give Z-Pal-NMeBzl, which was deprotected and the resulting H-Pal-NMeBzl was condensed with BOC-(2S,4R)-hydroxyproline to give H-Hyp-Pal-NMeBzl, which was acylated with indol-3-ylcarbonyl chloride to give the title compound II. Some **pharmaceutical** compns. containing I are described.

L26 ANSWER 26 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1994:533976 HCAPLUS
DOCUMENT NUMBER: 121:133976
TITLE: Carboxylic Acid Derivatives and Their Uses as **Pharmaceuticals**
INVENTOR(S): **Himmelsbach, Frank**; Linz, Guenter; Austel, Volkhard; Pieper, Helmut; Mueller, Thomas; Weisenberger, Johannes; Guth, Brian
PATENT ASSIGNEE(S): Thomae, Dr. Karl, G.m.b.H., Germany
SOURCE: Ger. Offen., 24 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4241632	A1	19940616	DE 1992-4241632	19921210 <--
CA 2111035	AA	19940611	CA 1993-2111035	19931208 <--
EP 604800	A1	19940706	EP 1993-119786	19931208 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
FI 9305513	A	19940611	FI 1993-5513	19931209 <--
NO 9304501	A	19940613	NO 1993-4501	19931209 <--
JP 06239817	A2	19940830	JP 1993-308419	19931209 <--

ZA 9309230	A	19950609	ZA 1993-9230		19931209 <--
AU 9352306	A1	19940623	AU 1993-52306		19931210 <--
CN 1094035	A	19941026	CN 1993-120876		19931210 <--
PRIORITY APPLN. INFO.:			DE 1992-4241632	A	19921210
OTHER SOURCE(S):	MARPAT 121:133976				

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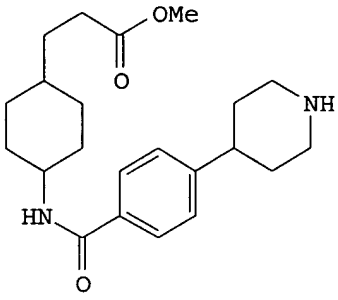

I

AB **Pharmacol.** active carboxylates were disclosed. A specifically claimed example compound, Me trans-4-[[4-(4-piperidinyl)phenyl]carbonylamino]cyclohexanepropanoate (I) was prepared The claimed compds. are blood platelet aggregation inhibitors (antithrombotics).

L26 ANSWER 27 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:	1994:269851 HCAPLUS
DOCUMENT NUMBER:	120:269851
TITLE:	Biphenyl derivatives, **drugs** containing them, and their preparation
INVENTOR(S):	Pieper, Helmut; **Himmelsbach, Frank**; Linz, Guenter; Austel, Volkhard; Mueller, Thomas; Weisenberger, Johannes
PATENT ASSIGNEE(S):	Dr. Karl Thomae GmbH, Germany
SOURCE:	Ger. Offen., 24 pp. CODEN: GWXXBX
DOCUMENT TYPE:	Patent
LANGUAGE:	German
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4219158	A1	19931216	DE 1992-4219158	19920611 <--
EP 574808	A1	19931222	EP 1993-109190	19930608 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
CA 2098158	AA	19931212	CA 1993-2098158	19930610 <--
NO 9302120	A	19931213	NO 1993-2120	19930610 <--
CN 1080917	A	19940119	CN 1993-106962	19930610 <--
JP 06073038	A2	19940315	JP 1993-138438	19930610 <--
ZA 9304090	A	19941211	ZA 1993-4090	19930610 <--
AU 9341201	A1	19931223	AU 1993-41201	19930611 <--
PRIORITY APPLN. INFO.:			DE 1992-4219158 A	19920611
OTHER SOURCE(S):	MARPAT 120:269851			

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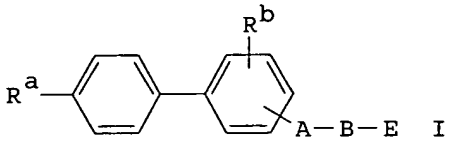

I

AB Title compds. I [Ra = an amidino group, if necessary substituted by an R1CO2(R2CR3)O2C, alkoxycarbonyl, phenylalkoxycarbonyl, alkenyloxycarbonyl, or phenylalkenyloxycarbonyl group; if E = carboxy or alkoxycarbonyl group with 2 or 3 C atoms or benzyloxycarbonyl, then the Ra amidino group is not substituted by an alkoxycarbonyl group with 2 or 3 C atoms or a benzyloxycarbonyl group; R1 = C1-5 alkyl, alkoxy, C5-7 cycloalkyl, cycloalkoxy, phenylalkyl, phenylalkoxy, Ph, PhO; R2 = H, C1-6 alkyl, C3-7 cycloalkyl, Ph; R3 = H, C1-6 alkyl; Rb = H, alkyl, OH, alkoxy; A = bond, CH2, CO, CH2CO, OCH2CO, where the latter 2 are joined to B through the CO; B = NR4CH2CH2X(CH2)n, where X = bond or HCR5 or NR5 group, NR4CH2CH2CR6:CH, NR4CO(CH2)m, or Y-W group; Y = NR4 or S when A = bond, n = 0, 1; m = 2-5; R4 = H, alkyl, phenylalkyl; R5 = H; or R4 and R5 or R4 and R6 together are an ethylene group; W = straight-chain C2-5 alkylene group, 1,4-cyclohexylene, etc.; E = carboxy, C2-7 alkoxycarbonyl, C8-10 **bicycloalkoxycarbonyl**, R1CO2(R2CR3)O2C; pyrrolidinyl, piperidinyl, morpholinyl, N-alkylpiperazinyl, etc.] are claimed, along with their stereoisomers, including mixts. thereof, their salts, especially physiol. compatible salts with inorg. or organic acids or bases, as aggregation-inhibiting **drugs** (no data), and their preparation For example, reaction of crude 4-cyano-4'-iodomethylbiphenyl (preparation given from 2.4 g 4-chloromethyl-4'-cyanobiphenyl) with 2.5g Me piperidinoacetate hydrochloride and 2.57 g Et3N in CHCl3 gave 59.6% 4-cyano-4'-[4-(methoxycarbonylmethyl)piperidinomethyl]biphenyl, which in turn was converted to the corresponding amidine and saponified to give 4-amidino-4'-[4-(carboxymethyl)piperidinomethyl]biphenyl; reaction of the latter with cyclohexanol in CH2Cl2 saturated with HCl gave 83.1% 4-amidino-4'-[4-(cyclohexyloxycarbonylmethyl)piperidinocarbonyl]biphenyl hydrochloride, the free base of which is claimed.

L26 ANSWER 28 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1994:77038 HCAPLUS
DOCUMENT NUMBER: 120:77038
TITLE: Novel amidine derivatives, their preparation, and their use as **medicaments** with LTB4-antagonistic effect
INVENTOR(S): Anderskewitz, Ralf; Schromm, Kurt; Renth, Ernst Otto; **Himmelsbach, Frank**; Birke, Franz; Fuegner, Armin
PATENT ASSIGNEE(S): Boehringer Ingelheim International G.m.b.H., Germany; Boehringer Ingelheim K.-G.
SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9316036	A1	19930819	WO 1993-EP70	19930114 <--

W: AU, CA, CZ, FI, HU, JP, KR, NO, NZ, PL, RU, SK, UA, US

RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
DE 4203201	A1	19930812	DE 1992-4203201	19920205	<--
DE 4224289	A1	19940127	DE 1992-4224289	19920723	<--
DE 4244241	A1	19940630	DE 1992-4244241	19921224	<--
AU 9333497	A1	19930903	AU 1993-33497	19930114	<--
AU 673343	B2	19961107			
EP 625138	A1	19941123	EP 1993-902195	19930114	<--
EP 625138	B1	19990602			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE					
JP 07503718	T2	19950420	JP 1993-513701	19930114	<--
JP 3487851	B2	20040119			
PL 173789	B1	19980430	PL 1993-304713	19930114	<--
PL 173781	B1	19980430	PL 1993-316750	19930114	<--
PL 173780	B1	19980430	PL 1993-316751	19930114	<--
SK 281016	B6	20001009	SK 1994-914	19930114	
FI 9403618	A	19940804	FI 1994-3618	19940804	<--
NO 9402903	A	19941003	NO 1994-2903	19940804	<--
FI 2000002501	A	20001115	FI 2000-2501	20001115	
PRIORITY APPLN. INFO.:			DE 1992-4203201	A 19920205	
			DE 1992-4224289	A 19920723	
			DE 1992-4244241	A 19921224	
			WO 1993-EP70	A 19930114	

OTHER SOURCE(S): MARPAT 120:77038

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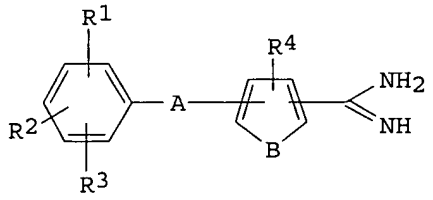

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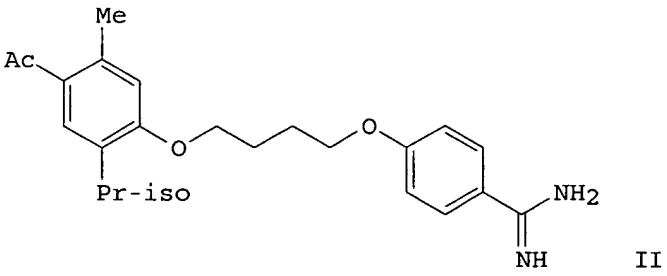

II

AB Amidines I [R1, R2, R3 = wide variety of groups; or adjacent R1R2 = (un)substituted CH:CHCH:CH, OCH2CH2, OCH2O, OCH2CH2O, (CH2)3-4, NHCO2, NHCOCH2O, COCH2O, COCH2CH2O; R4 = halo, (di)(alkyl)amino, OH, alkoxy; A = X1A1X2, X2A2X3, X4A2X2, OC6H4O, 1,4-piperazinediyl (Q), etc.; B = CH:CH, CH:N, S, o-C6H4; A1 = C2-4 alkylene, CH2CH:CHCH2, CH2C.tplbond.CCH2, Q1, CH2Q1CH2, (Q1 = cyclohexanediyl), etc.; A2 = C1-5 alkylene; X1 = O, NH, S, SO, SO2, CO, CH2, Q; X2 = O, NH, S, OC6H4; X3 = NHCO, CONH, SO2NH, Q; X4 = NHCO, CONH, NHSO2, SO2NH, NHCONH] and their salts were prepared as LTB4 antagonists, for treatment of inflammatory and/or allergic conditions. For example, 4-[(4-acetyl-2-isopropyl-5-methylphenoxy)butyloxy]benzonitril e underwent Pinner reaction (i.e., HCl in EtOH to give the imidate ester

hydrochloride, and subsequent ammonolysis of this with 5M NH3 in EtOH) to give amidine salt II-HCl. Several tested I inhibited binding of [3H]-LTB4 to live U937 cell receptors (Ki = 1.7-15.0 nM), inhibited LTB4-induced guinea-pig neutrophil aggregation in vitro (EC50 = 0.02-1.9 μM), and inhibited LTB4-induced neutrophil accumulation in ears of mice (p.o. ED50 = 0.8-3.8 mg/kg).

L26 ANSWER 29 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1993:560274 HCAPLUS
DOCUMENT NUMBER: 119:160274
TITLE: Preparation of 5-membered heterocycles for antithrombotic and fibrinogen-binding activity.
INVENTOR(S): **Himmelsbach, Frank**; Linz, Guenter; Austel, Volkhard; Pieper, Helmut; Mueller, Thomas; Weisenberger, Johannes; Seewaldt-Becker, Elke
PATENT ASSIGNEE(S): Thomae, Dr. Karl, G.m.b.H., Germany
SOURCE: Ger. Offen., 39 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4124942	A1	19930128	DE 1991-4124942	19910727 <--
EP 525629	A2	19930203	EP 1992-112568	19920722 <--
EP 525629	A3	19970319		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, PT, SE				
CA 2074685	AA	19930128	CA 1992-2074685	19920724 <--
NO 9202940	A	19930128	NO 1992-2940	19920724 <--
HU 61747	A2	19930301	HU 1992-2450	19920724 <--
JP 05221999	A2	19930831	JP 1992-198359	19920724 <--
ZA 9205573	A	19940124	ZA 1992-5573	19920724 <--
IL 102638	A1	19961016	IL 1992-102638	19920724 <--
AU 9220569	A1	19930128	AU 1992-20569	19920727 <--
AU 652064	B2	19940811		
US 5463071	A	19951031	US 1993-148724	19931108 <--

PRIORITY APPLN. INFO.: DE 1991-4124942 A 19910727
US 1992-919343 B1 19920723

OTHER SOURCE(S): MARPAT 119:160274
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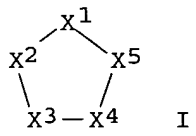

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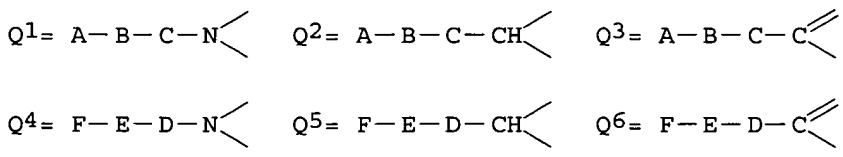

AB Title compds. [I; one of X1-X5 = Q1-Q3, a second = Q4-Q6, a third = S, SO, N, R1N, R2C, (R2)2C, a fourth = O, S, N, SO2, R2C, CO, and a fifth = R2C,

(R2)2C, N; A = cyano, (substituted) amino, aminoalkyl, amidino, guanidino; B = bond, alkylene, (substituted) phenylene, pyridinylene, pyrazinylene, triazinylene, etc.; C = (substituted) phenylene, pyridinylene, pyrimidinylene, pyrazinylene, pyridazinylene, triazinylene, cycloalkylene; D = (substituted) alkylene, alkenylene, phenylene, pyridinylene, pyrimidinylene, pyrazinylene, pyridazinylene, triazinylene, cycloalkylene, etc.; E = bond, alkylene, etc.; F = carboxy, (substituted) alkoxycarbonyl; R1 = H, alkyl, aralkyl, aryl, heteroaryl; R2 = H, Cl, Br, alkyl, aralkyl, aryl, heteroaryl, alkoxy, R1O2C, (R1)2N, etc.]. Thus, 1-[6-(4-amidinophenyl)-3-pyridazinyl]-4-(2-carboxyethyl)imidazole, prepared via saponification of the corresponding Me ester, showed IC50 = 73 nM in a screen for binding of fibrinogen to human thrombocytes.

L26 ANSWER 30 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1993:539078 HCAPLUS
DOCUMENT NUMBER: 119:139078
TITLE: Preparation of 5-[(aminoaryloxy)methyl]-2-pyrrolidinoneacetates and analogs as **drugs**
INVENTOR(S): **Himmelsbach, Frank**; Austel, Volkhard; Pieper, Helmut; Eisert, Wolfgang; Mueller, Thomas; Weisenberger, Johannes; Linz, Guenter; Krueger, Gerd
PATENT ASSIGNEE(S): Thomae, Dr. Karl, G.m.b.H., Germany
SOURCE: Eur. Pat. Appl., 173 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 483667	A2	19920506	EP 1991-118148	19911024 <--
EP 483667	A3	19920916		
EP 483667	B1	19980204		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
DE 4035961	A1	19920507	DE 1990-4035961	19901102 <--
AT 163008	E	19980215	AT 1991-118148	19911024 <--
ES 2113867	T3	19980516	ES 1991-118148	19911024 <--
SG 81852	A1	20010724	SG 1996-1241	19911024
FI 9105136	A	19920503	FI 1991-5136	19911031 <--
FI 107606	B1	20010914		
CA 2054850	AA	19920503	CA 1991-2054850	19911101 <--
CA 2054850	C	20010102		
NO 9104294	A	19920504	NO 1991-4294	19911101 <--
NO 174806	B	19940405		
NO 174806	C	19940713		
AU 9186926	A1	19920507	AU 1991-86926	19911101 <--
AU 650488	B2	19940623		
JP 04264068	A2	19920918	JP 1991-313154	19911101 <--
JP 2937589	B2	19990823		
HU 67288	A2	19950328	HU 1991-3455	19911101 <--
RU 2040519	C1	19950725	RU 1991-5001905	19911101 <--
IL 99926	A1	19960618	IL 1991-99926	19911101 <--
KR 223135	B1	19991015	KR 1991-19458	19911102
ZA 9108734	A	19930504	ZA 1991-8734	19911104 <--
US 5541343	A	19960730	US 1994-365336	19941228 <--
US 5591769	A	19970107	US 1995-458096	19950601 <--
PRIORITY APPLN. INFO.:			DE 1990-4035961 A	19901102
			US 1991-783065 B1	19911025

US 1994-365336 A3 19941228

OTHER SOURCE(S): MARPAT 119:139078

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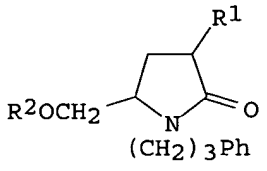

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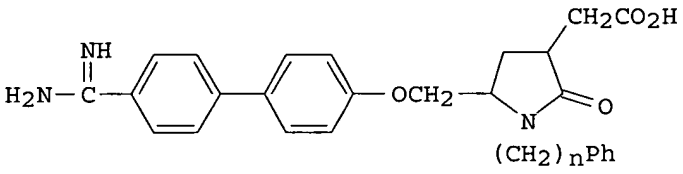

III

AB Compds. BXAYE [A = 4- to 7-membered (substituted) alkyleneiminodiyl; B = cyano, NO2, NH2, C(:NH)NH2, NHC(:NH)NH2, etc.; E = vinyl, CH2OH, cyano, SO2H, CO2H, alkoxycarbonyl, etc.; X = X5X4X3X2X1; X1 = bond, alkylene, or arylene which may be linked to X2 by O, SO2, CO, etc.; X2 = fluorenylene, arylene, hydronaphthaleneylene, etc.; X3, X5 = bond, (unsatd.) alkylene, etc.; X4 = bond, arylene, (bi)cycloalkylene; Y = Y1Y2Y3; Y1, Y2 = bond, (unsatd.) alkylene, etc.; Y3 = bond, arylene, alkylenearylene, etc.] were prepared Thus, (S)-5-[(trityloxy)methyl]-2-pyrrolidinone was condensed with Ph(CH2)3Br and the product alkylated with BrCH2CH:CH2 to give, after deprotection and mesylation, pyrrolidinone (3R,5S)-I (II; R1 = CH2CH:CH2, R2 = SO2Me) which was condensed with 4'-cyano-4-hydroxybiphenyl to give, after oxidation and esterification, II (R1 = CH2CO2Me, R2 = 4'-cyano-4-biphenylyl). The latter was converted in 2 steps to title compound (3R,5S)-III (IV; n = 3). IV (n = 0) had IC50 of 0.024 μM against binding of fibrinogen to human thrombocytes in vitro.

L26 ANSWER 31 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1993:495524 HCAPLUS
DOCUMENT NUMBER: 119:95524
TITLE: Preparation of condensed 5-membered heterocycles as **drugs**
INVENTOR(S): Austel, Volkhard; Pieper, Helmut; **Himmelsbach, Frank**; Linz, Guenter; Mueller, Thomas; Weisenberger, Johannes; Seewaldt-Becker, Elke
PATENT ASSIGNEE(S): Thomae, Dr. Karl, G.m.b.H., Germany
SOURCE: Ger. Offen., 32 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4129603	A1	19930311	DE 1991-4129603	19910906 <--
US 5434150	A	19950718	US 1992-937914	19920828 <--
EP 531883	A1	19930317	EP 1992-115057	19920903 <--

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE						
CA 2077577	AA	19930307	CA 1992-2077577		19920904	<--
NO 9203466	A	19930308	NO 1992-3466		19920904	<--
AU 9222178	A1	19930311	AU 1992-22178		19920904	<--
AU 657350	B2	19950309				
HU 61984	A2	19930329	HU 1992-2857		19920904	<--
JP 06025181	A2	19940201	JP 1992-237334		19920904	<--
ZA 9206700	A	19940304	ZA 1992-6700		19920904	<--
RU 2041211	C1	19950809	RU 1992-5052824		19920904	<--
IL 103053	A1	19960804	IL 1992-103053		19920904	<--
PRIORITY APPLN. INFO.:			DE 1991-4129603	A	19910906	
OTHER SOURCE(S):	MARPAT 119:95524					

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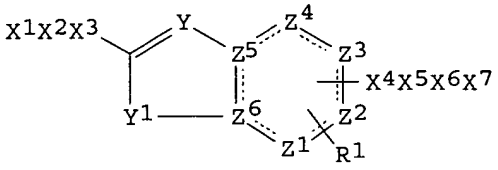

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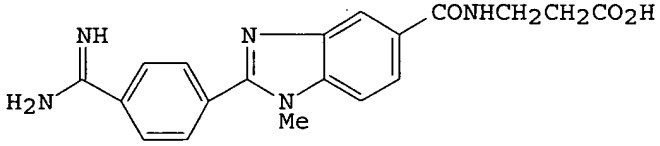


II

AB Title compds. [I; R1 = H, F, Cl, Br, alkyl, aralkyl, aryl, heteroaryl, R3O, (R3)2N, R3CONR3, R3S, R3SO, R3SO2, R4, etc.; R3 = H, alkyl, aryl, heteroaryl, aralkyl; R4 = azetidino, pyrrolidino, hexamethyleneimino, heptamethyleneimino, (modified) (substituted) piperidino; Y = NO, N, (alkyl)methine, Y1 = O, S, N, imino; Z1-Z4 = C, methine, imino, N; Z5, Z6 = C, N; X1 = cyano, (substituted) amino, aminoalkyl, amidino, guanidino, guanidinoalkyl; X2 = (substituted) (modified) phenylene, cycloalkylene; X3 = bond, (modified) alkylene; X4 = alkylene, bond; X5 = alkylene, alkenylene, alkynylene, O, S, SO, SO2, NR3, NCOR3, CO, NR3CO, SO2NR3, etc.; X6 = bond, alkylene, alkenylene, alkynylene, cycloalkylene, alkylenecycloalkylene; X7 = CO2H, (substituted) alkoxycarbonyl, sulfo, phosphono, alkylphosphono, tetrazolyl; with provisos], were prepared as inhibitors of inflammation, bone degradation, thrombosis, cell aggregation, neoplasms, and metastasis. Thus, title compound II inhibited collagen-induced platelet aggregation with EC50 = 70 nM, and inhibited binding of fibrinogen to human erythrocytes with IC50 = 37 nM.

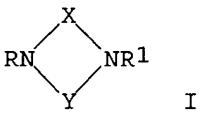
L26 ANSWER 32 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:	1993:101980 HCAPLUS
DOCUMENT NUMBER:	118:101980
TITLE:	Preparation of cyclic ureas as cell-cell and cell-matrix interaction inhibitors
INVENTOR(S):	**Himmelsbach, Frank**; Pieper, Helmut; Austel, Volkhard; Linz, Guenter; Mueller, Thomas; Weisenberger, Johannes; Eisert, Wolfgang
PATENT ASSIGNEE(S):	Thomae, Dr. Karl, G.m.b.H., Germany
SOURCE:	Eur. Pat. Appl., 91 pp. CODEN: EPXXDW
DOCUMENT TYPE:	Patent

LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE	
EP 503548	A1	19920916	EP 1992-104045		19920310	<--
EP 503548	B1	19970604				
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, PT, SE						
DE 4107857	A1	19920917	DE 1991-4107857		19910312	<--
FI 9201030	A	19920913	FI 1992-1030		19920310	<--
AT 154013	E	19970615	AT 1992-104045		19920310	<--
ES 2104754	T3	19971016	ES 1992-104045		19920310	<--
CA 2062655	AA	19920913	CA 1992-2062655		19920311	<--
NO 9200957	A	19920914	NO 1992-957		19920311	<--
AU 9212803	A1	19920917	AU 1992-12803		19920311	<--
AU 654340	B2	19941103				
HU 60722	A2	19921028	HU 1992-823		19920311	<--
ZA 9201804	A	19930913	ZA 1992-1804		19920311	<--
IL 101203	A1	19951231	IL 1992-101203		19920311	<--
JP 04368372	A2	19921221	JP 1992-53171		19920312	<--
PRIORITY APPLN. INFO.:			DE 1991-4107857	A	19910312	
OTHER SOURCE(S):	MARPAT 118:101980					

GI



I

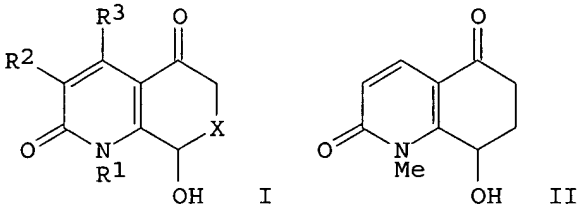
AB Title compds. [I; X = CO, CS, SO, SO2, (substituted) carbimino; Y = (R2, R3-substituted) C2-4 alkylene, alkenylene, C4-7 cycloalkenylene, CONH, CH:N, etc.; one of R-R3 = A-B-C; A = (substituted) aminoalkyl, amino, amidino, guanidino, cyano, cyanoalkyl; B = bond, alkylene, alkenylene, (substituted) phenylene, pyridinylene, pyrimidinylene, pyrazinylene, cyclopropylene, biphenylene, etc.; C = (substituted) alkylene, alkenylene, alkylenecarbonyl, phenylene, indanylene, tetrahydronaphthalenediyl, pyridinylene, pyrimidinylene, pyrazinylene, pyridazinylene, triazinylene, cycloalkylene, etc.; another of R-R3 = F-E-D; D = alkylene, alkenylene, (substituted) phenylene, pyridinylene, pyrimidinylene, pyrazinylene, pyridazinylene, triazinylene, cycloalkylene, etc.; E = bond, (substituted) alkylene, phenylene, pyridinylene, pyrimidinylene, pyrazinylene, pyridazinylene, triazinylene, cycloalkylene, etc.; F = CO2H, (substituted) alkoxycarbonyl; the third of R-R3 = H, alkyl, perfluoroalkyl, aralkyl, (hetero)aryl, etc.; the fourth of R-R3 = H, alkyl, aralkyl, aryl, heteroaryl; RR2, RR3, R1R2, R1R3 = bond], were prepared Thus, 1-(4'-amidino-4-biphenylyl)-3-methoxycarbonylmethylimidazolidin-2-one hydrochloride was stirred with 1N NaOH in MeOH to give 1-(4'-amidino-4-biphenylyl)-3-carboxymethylimidazolidin-2-one. I inhibited collagen-induced blood platelet aggregation with IC50 = 30 - >100,000 nM. Generic **drug** formulations are given.

L26 ANSWER 33 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1991:449427 HCAPLUS
DOCUMENT NUMBER: 115:49427
TITLE: Preparation and formulation of 8-hydroxy-quinolin-2,5-diones as analgesics, antiinflammatories, and

antipyretic agents
INVENTOR(S): Schmid, Jochen; Engelhardt, Guenther; Prox, Axel; Heckel, Armin; **Himmelsbach, Frank**
PATENT ASSIGNEE(S): Thomae, Dr. Karl, G.m.b.H., Germany
SOURCE: Ger. Offen., 9 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3927609	A1	19910228	DE 1989-3927609	19890822 <--

PRIORITY APPLN. INFO.: DE 1989-3927609 19890822
OTHER SOURCE(S): MARPAT 115:49427
GI



AB The title compds. [I; R1 = H, (cyclo)alkyl, alkynyl, alkoxyalkyl, (un)substituted Ph, etc.; R2 = H, alkyl; R3 = H, CF3, Ph, alkyl; R2R3 = (CH2)3-5; X = (di)(alkyl)methylene] were prepared Thus, 1-methyl-7,8-dihydro-2,5(1H,6H)quinolinedione was refluxed with NBS and HIBN in CHCl3/CCl4 and the product stirred with Ag2CO3 in aqueous Me2CO to give title compound II which had ED50 of 19.9 and 14.4 mg/kg intragastrically against s.c. yeast-induced pain in rats at 45 and 90 min, resp. **Pharmaceutical** formulations comprising I are given.

L26 ANSWER 34 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1985:142744 HCAPLUS
DOCUMENT NUMBER: 102:142744
TITLE: A new monooxygenase product from 7-ethoxycoumarin and its relation to the O-dealkylation reaction
AUTHOR(S): **Jung, Birgit**; Graf, Hermann; Ullrich, Volker
CORPORATE SOURCE: Fak. Biol., Univ. Konstanz, Konstanz, D-7750, Fed. Rep. Ger.
SOURCE: Biological Chemistry Hoppe-Seyler (**1985**), 366(1), 23-31
CODEN: BCHSEI; ISSN: 0177-3593
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The widely used fluorometric microsomal monooxygenase test for 7-ethoxycoumarin [31005-02-4] O-dealkylation was reinvestigated with regard to other possible hydroxylation products. By HPLC-anal. no β-hydroxylation of the Et group and no 8-hydroxylation could be detected. Only a small percentage of 6-hydroxylation occurred, but as a new major metabolite 7-ethoxy-3-hydroxycoumarin [95633-01-5] was found in

quantities depending on the microsomal preparation used. The isozyme mainly responsible for 3-hydroxylation exhibited a great dependence on cytochrome b5 [9035-39-6]. The fluorometric test does not include 3-hydroxylation due to the virtual absence of an emission spectrum above 450 nm. Therefore, to determine total monooxygenase patterns of 7-ethoxycoumarin, a chromatog. separation of the products is required. Large variations in monooxygenase product pattern were observed with different inducers, pH, and buffers. Thus, if monooxygenase product pattern from ethoxycoumarin are used for the characterization of cytochrome P 450 isozymes, the conditions of the medium should be carefully controlled.

L26 ANSWER 35 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1984:205822 HCAPLUS
DOCUMENT NUMBER: 100:205822
TITLE: Evidence for a propulsive function of the migrating myoelectric complex in rats
AUTHOR(S): Wilen, T.; Gustavsson, S.; **Jung, B.**
CORPORATE SOURCE: Dep. Surg. Radiophys., Univ. Hosp., Uppsala, S-750 14, Swed.
SOURCE: European Surgical Research (**1984**), 16(2), 113-19
CODEN: EUSRBM; ISSN: 0014-312X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB To investigate the relation between myoelec. activity and the transport of small bowel luminal contents, recordings of migrating myoelec. complexes (MMCs) were combined with studies of the propulsion of a bile-excreted radioactive test substance. At laparotomy, rats were provided with 3 pairs of bipolar electrodes, sewn to the seromuscular layer of the small bowel 15, 30, and 45 cm distal to the pylorus. After recovery for 1 wk, MMCs were recorded with the animal fasted for 18 h and in light barbiturate anesthesia. Concurrently, the bile-excreted **radiopharmaceutical**, 99mTc-HIDA, was infused i.v. At the end of the experiment, the rats were sacrificed and the distribution of 99mTc activity was recorded from the excised bowel specimen. In 12 animals with a typical MMC activity recurring every 20 min, the small bowel radioactivity was distributed into discrete portions, separated by fairly long empty segments. In 6 animals, the expts. were terminated when an MMC activity front had reached 1 of the electrodes and in all, a portion of radioactivity was located immediately distal to the position of that particular electrode. Control animals were killed when .apprx.10 min had elapsed since the MMC front passed 1 of the electrode sites. In all these cases, the electrode position corresponded to empty bowel segments. These data obtained from animals with permanent electrodes but an otherwise intact small bowel strongly support the notion that MMCs result in propulsion of luminal contents.

L26 ANSWER 36 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1981:491144 HCAPLUS
DOCUMENT NUMBER: 95:91144
TITLE: Kidney radioprotection by temporary hypoxia. Experiments with degradable microspheres
AUTHOR(S): Forsberg, J. O.; Hillered, L.; Graffman, S.; **Jung, B.**; Persson, E.; Selen, G.
CORPORATE SOURCE: Dep. Surg., Akad. Sjukhuset, Uppsala, Swed.
SOURCE: Scandinavian Journal of Urology and Nephrology (**1981**), 15(2), 147-52
CODEN: SJUNAS; ISSN: 0036-5599
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Deep hypoxia protects biol. tissue against ionizing radiation. By intra-arterial injection of degradable starch microspheres, the renal circulation was temporarily blocked in unilaterally nephrectomized rats. The induced hypoxia was utilized for protection of the kidney against single doses of high-voltage x-rays. Renal function and survival date were compared between animals protected by hypoxia and nonprotected animals. The survival rate of the former animals exceeded that of the latter by a factor of 1.6. All irradiated animals showed a lower glomerular filtration rate, Hippuran clearance, and urine osmolarity than nonirradiated controls. Surviving, protected animals irradiated with 42 and 52 Gy showed a glomerular filtration of .apprx.0.5 mL/min and a Hippuran clearance of .apprx.2 mL/min, whereas all nonprotected animals irradiated with 42 Gy died.

L26 ANSWER 37 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1978:579598 HCAPLUS
DOCUMENT NUMBER: 89:179598
TITLE: Scope of the homo-Diels-Alder reaction
AUTHOR(S): Fickes, Garry N.; **Metz, Thomas E.**
CORPORATE SOURCE: Dep. Chem., Univ. Nevada, Reno, NV, USA
SOURCE: Journal of Organic Chemistry (1978), 43(21), 4057-61
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The reactivity of **bicyclo**[2.2.2]octa-2,4-diene, **bicyclo**[3.2.2]nona-6,8-diene, and 3,3-dimethyl-1,4-pentadiene in the homo-Diels-Alder reaction was investigated as an assessment of the scope of this reaction. The scope is rather limited, with the efficiency of the diene in the reaction generally being related to the distance between the double bonds.

L26 ANSWER 38 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1972:3037 HCAPLUS
DOCUMENT NUMBER: 76:3037
TITLE: Scope of the homo Diels-Alder reaction
AUTHOR(S): **Metz, Thomas E.**
CORPORATE SOURCE: Univ. Nevada, Reno, NV, USA
SOURCE: (1971) 113 pp. Avail.: Univ. Microfilms, Ann Arbor, Mich., Order No. 71-18,647
From: Diss. Abstr. Int. B 1971, 32(1), 177
DOCUMENT TYPE: Dissertation
LANGUAGE: English
AB Unavailable

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